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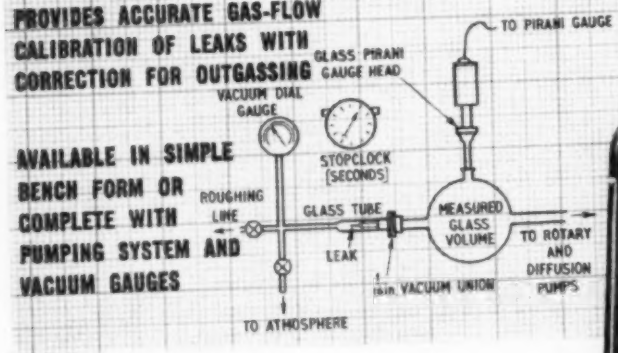

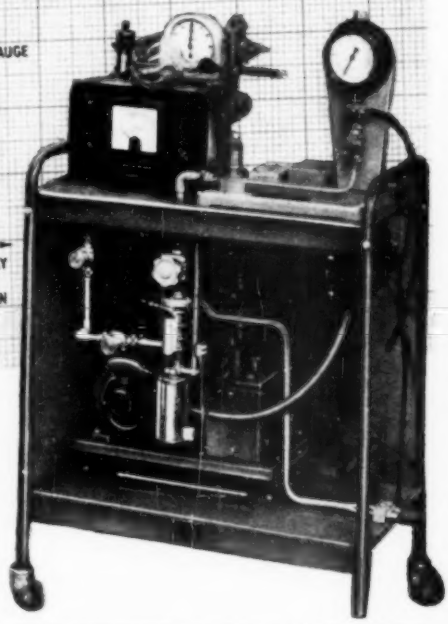

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* 1 lusec = 1 litre micron/second.

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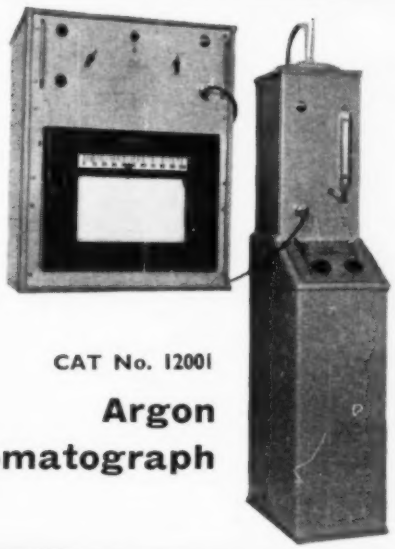

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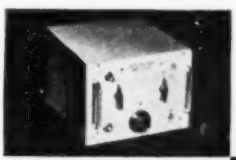

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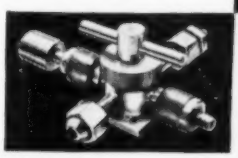

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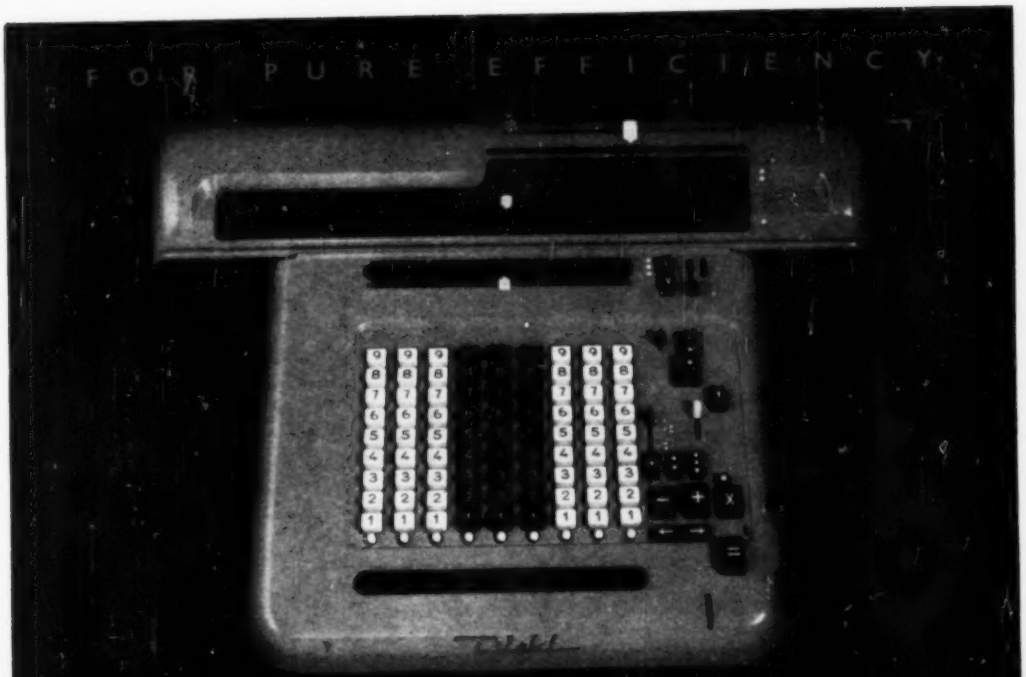

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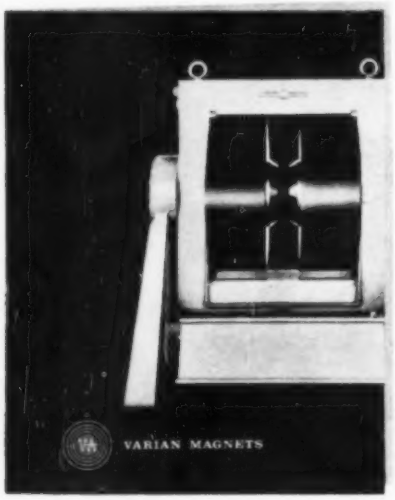

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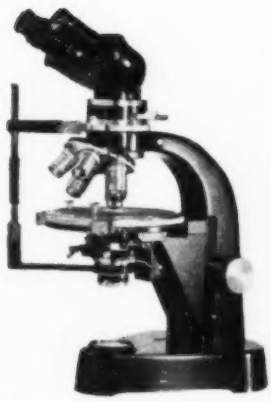

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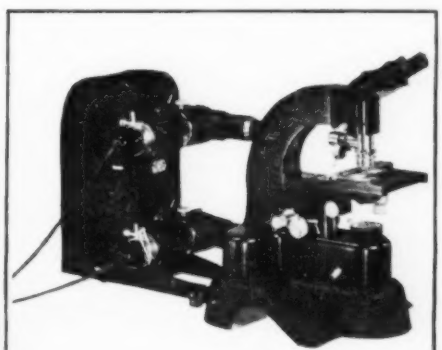

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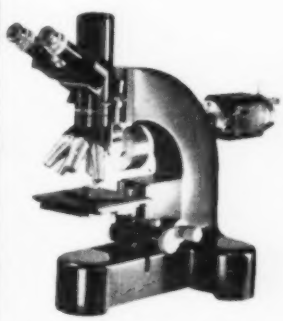

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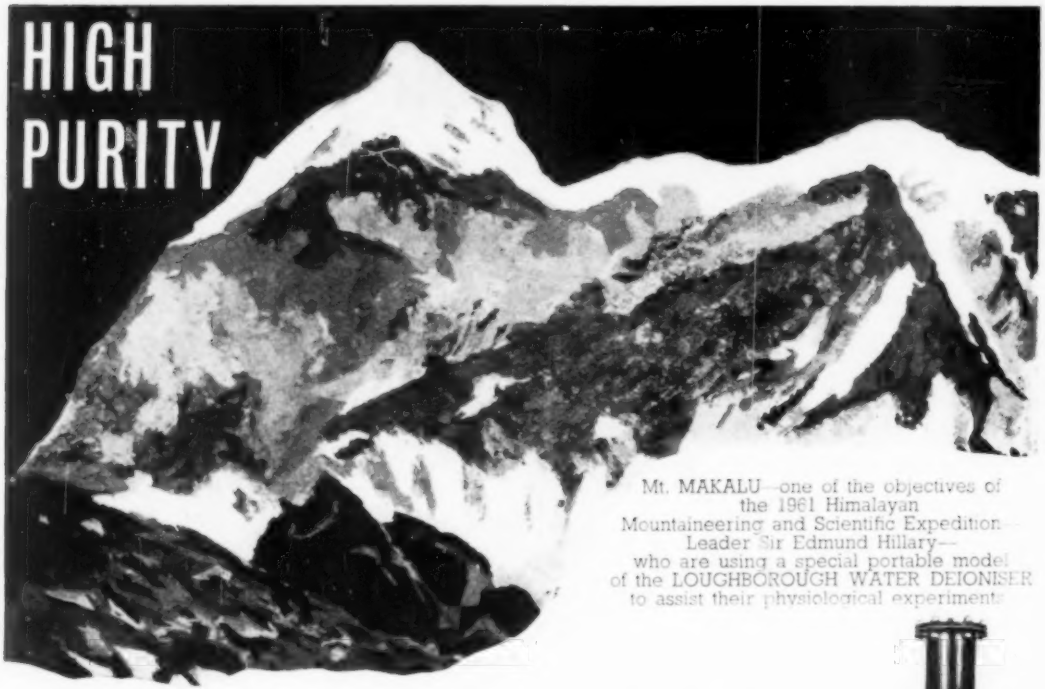

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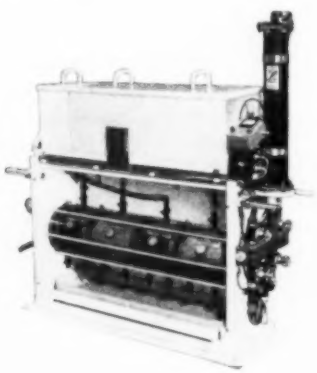

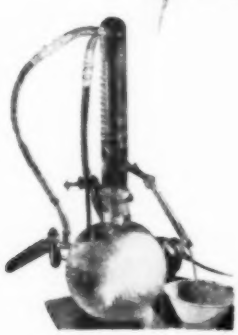

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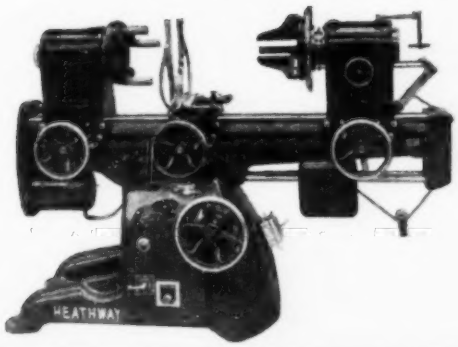

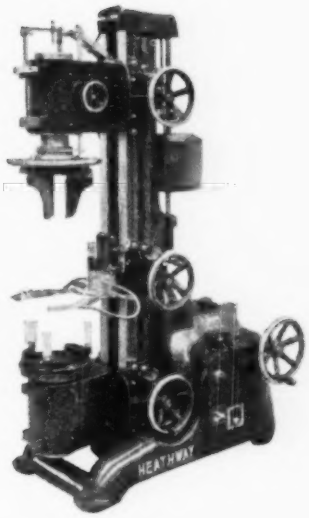

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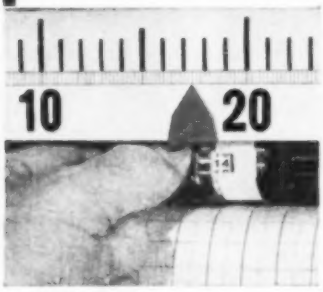

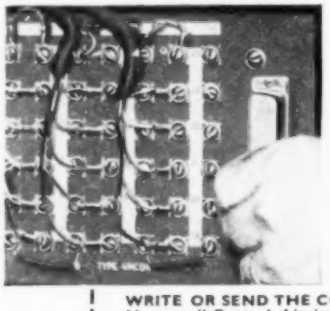

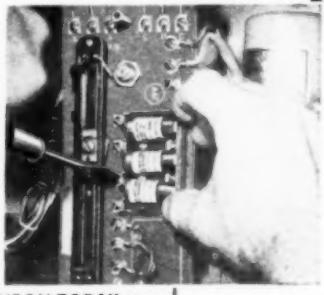

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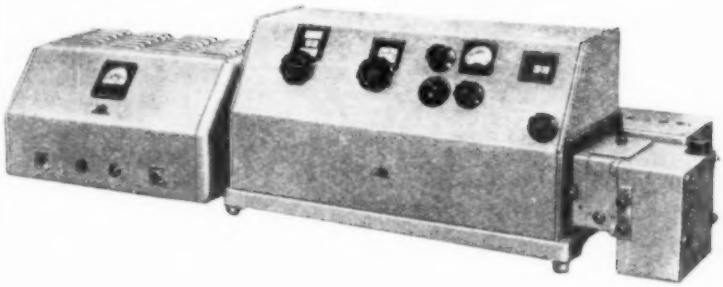

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EDUCATING THE WHOLE MAN

IN his address as 'special visitor' at the commemoration day ceremonies of the Imperial College of Science and Technology, Sir Cyril Hinshelwood once again affirmed his disbelief in the 'two cultures'. He thinks instead that there are simply two attitudes, and that it is the business of universities to encourage the right attitude. Addressing more particularly the younger part of his audience, he proceeded to outline constructively what he meant by the right attitude and how it could be developed.

It is interesting to set Sir Cyril's address beside Sir Mark Oliphant's Frank Tate Memorial Lecture on science and ethics recently delivered at the University of Melbourne and published in the quarterly *Overland*. Sir Mark began by referring to Sir Charles Snow's Rede Lecture, and while he himself is disposed to admit the existence of a gulf between two cultures, he was no less forthright than Sir Cyril in condemning the educational methods that are responsible for perpetuating such a gulf between the scientific disciplines and the humanities. In Australia, there are, Sir Mark said, continual and confused complaints of falling standards in the teaching of science in schools, due to the difficulty in obtaining the services of good science masters: and the catastrophic result, he said, of the determination of Asian nations to become technologically industrialized in the minimum of time is apparent to all who have examined the schools and universities in those countries. The educational processes through which men pass, from the kindergarten to the university, deliberately preserve the schism in Western culture, and it often seemed to Sir Mark that there is a conspiracy among educationists to create and widen a gap between the two aspects of our culture.

Sir Mark Oliphant thinks that, unfortunately, those who strive most assiduously to make this chasm unbridgeable are the humanists, who continue to fight a rearguard action against science instead of endeavouring to change it into a full and satisfying part of cultural education, such as Sir Cyril Hinshelwood and Sir Eric Ashby, for example, have claimed that it can be. Scientists, on the other hand, Sir Mark believes, are largely either indifferent towards the humanities or are openly contemptuous of what they regard as the imprecision, the paucity of new ideas, and the accumulation and regurgitation of information. In consequence, for example, the philosopher may ignore the great wealth of precisely recorded experience which is science, while those in the faculties of science, technology and medicine are denied the questioning of the basis of their system of natural knowledge which a study of philosophy can contribute.

Sir Mark recognizes the grave threats to the continued existence of mankind which have come from scientific and technological advance; but though he points out that most of our beliefs and the attitudes which arise from them will not stand up to careful or inspired analysis, and that a completely rational world is neither a possibility nor a desirable state of affairs, he does not, like Prof. C. A. Coulson in his Beckley Lecture, pursue this to its conclusion. Nevertheless, like Prof. Coulson, he recognizes that only through education can we hope to convey to every man some understanding of science and the way it advances, so that he has some idea of the forces which shape his life and his destiny; and, again like Prof. Coulson, he comes down emphatically in support of making science as much a part of universal education as history or English, so that pupils accept the necessity of knowing something of the structure of the universe as readily as they accept the need for some knowledge of the geography of the world. With proper understanding of this greatest single problem in teaching and the boldness to tackle it experimentally, in whatever ways seem promising, Sir Mark believes the chasm between our two cultures could disappear in a single generation.

Here accordingly, though he began by seeking a rapid bridge of the gap, Sir Mark's thought approaches that of Sir Cyril Hinshelwood, and he believes, too, that science can, and should, be taught in such a way that even those who follow primarily totally different courses have enough knowledge to be sensible about, and sensitive to, the needs of the rapidly changing world in which they live. He does not, however, believe that education about science and the scientific point of view for the ordinary man and woman can be the same as education in science for the budding man of science, but that a totally different approach is required: and though he makes some important suggestions, on the whole his analysis is scarcely as penetrating as that of Sir Cyril Hinshelwood or Prof. Coulson. If science is to be taught as a general cultural subject in primary and secondary schools, knowledge of Nature, he urges, must be presented as a unity, and it is essential to preserve to the full the questioning, eager approach to the world which is natural in children, making it the very bedrock of the inquiry into Nature which a course in science should be. Every statement of fact should be justified by the evidence, and the real significance of the 'laws' of science, as reasonable approximations, to be discarded as better concepts are born, must be woven into all discussion of them.

Sir Mark points out, too, how science, taught in this way, displaying the contributions which all nations have made to the advancement of science, can help to dispel some of the illusions which feed nationalism: the idea that no knowledge can be secret, but that it only becomes knowledge when shared with and tested by others, is a lesson to be learnt as early as possible. Attacking the illusion that science is a second-rate discipline, he observes very pertinently that the number of scientists is now great enough for them to form a general cross-section of the community, and that among them accordingly

will be found the same fraction with the ability to lead, in industry or in government, as among those whose specialized knowledge is in law, history, the classics, economics or commerce. Perhaps a larger proportion of scientists is seriously concerned for the present well-being and the future of mankind, because they appreciate more clearly the realities of nuclear warfare, the nature of the population explosion which threatens our standards of living, and the subtle dangers of man's continuing interference with Nature.

It is essential that man should face up to all the grave responsibilities involved now that the biological future is in his hands, with the increasing effects of the extremely rapid development of ideas and knowledge on the evolution of his social systems, his problems of education and his religion. Sir Mark agrees with Anatol Rapoport that there exist in science ethical principles which are inherent in its pursuit and that there is something universally satisfying about the scientific point of view, particularly as it affects man's relation to his environment. The keystone of science is the pursuit of truth, and Sir Mark maintains in conclusion that the pursuit of knowledge is in no way incompatible with the preservation of human dignity, of the eternal values of art and literature, or with the ethical principles which must govern men's lives. Indeed, science has positive contributions to make to all human activities, and can uphold the basis of value judgments at a time when the religious authority for these is disintegrating.

That last proposition may be debatable, but nevertheless in his conclusion Sir Mark comes very close to both Sir Cyril Hinshelwood and Prof. Coulson, particularly when he pleads for re-thinking the whole basis of education, so that science and its relations with man may permeate the whole fabric of teaching and thus, as sufficient understanding of science and knowledge of its content becomes a natural part of the preparation of every man and woman for life, repair the rift existing between science and other forms of human culture. In his address at the Imperial College of Science and Technology, however, Sir Cyril Hinshelwood laid much less stress on formal teaching, though he agreed that there might be an optimum arrangement of the formal syllabus. The really essential thing is that what is studied at the university should become part of life and should be handled in such a way as to achieve this. The formal teaching, he said, is only a small part of what a university provides, and if the tone and atmosphere of a university are right, general reading, discussion, conversation and argument provide a good deal of the breadth which, as well as depth, is desirable in the educated man. In developing his argument that besides depth, or intensity of experience and technical proficiency, the educated man should seek first of all a broad vision of how his own subject fits into the scheme of things—and that the varied ways in which the painter, the historian, the biologist or the physicist looks at the world, all represent attempts to come to grips with the reality about us—Sir Cyril, by implication, refuted much that Dr. A. P. Rowe advocated about practices and changes in British universities in a recent broadcast talk, "Dry Rot and Redbrick", and which he has also expanded in an article, "The Problem of Freedom and Efficiency in Universities" in *Science and Freedom* for October. Sir Cyril was concerned quite clearly with the average student, not just with the *élite*, and with the teaching which should be given them; and though there is substance in the charges that there is too little scholarship, much trivial research and much waste of public money, Sir Cyril was not concerned directly with these questions. He was concerned that the student should receive a worthy education, and his conception of university teaching is the antithesis of Dr. Rowe's rejection of any idea of a broad education and his suggestion that research should be relegated to research institutes.

Sir Cyril Hinshelwood's reasoned exposition of his conception of the humane or liberal approach deserves careful study. He is convinced that while subjects will wax and wane in importance, and methods be introduced and superseded, there will always be the need to find some satisfaction and understanding in a broad view of the world, and in acquiring the expert skill by which somewhere the student can in due course make an effective contribution. Moreover, it is because he sees the relation of student and teacher in a university as one of partnership, of a guide, rather than oracle, that he maintains teaching and research must remain closely interlinked. In research new knowledge comes into being, and academic studies become part of real life. Work in the laboratory, he observed, with its hopes and disappointments, its difficult decisions when to continue and when to cut losses, its subtle dependence on human relations, is an education in life which the arts scarcely parallel. Finally, he rejected explicitly the idea that research should be concentrated in central institutes devoted solely to that end as likely to imperil the creative attitude, the sense of responsibility and involvement which are developed in the right university atmosphere.

Developing this theme, Sir Cyril pointed out that what we study, whether literature or science, is not part of life and is therefore not humane. How we study is part of life and therefore is humane, and he argued further that the right attitude to all affairs is fostered by the practice of the right approach to our subjects of study. The strenuous effort to see a subject in its true and wide perspective cultivates sanity of judgment in much broader fields. Independent thought, critical assessment of supposed authorities, and sharing of responsibility with our teachers for the views we adopt, engender a healthy mistrust of political pundits and foster the spirit of resistance to the endless petty tyrannies which beset modern life. In words which are echoed in the lectures by Sir Mark Oliphant and Prof. Coulson, Sir Cyril suggests that the need in science to reach one's ends by exacting and precise techniques, whether mathematical or experimental, is a great corrective of the tendency to airy generalization, which is

another weakness of the modern world: also that the independent, constructive and, in however modest a degree, creative approach to a subject is the best guarantee that those who have passed through a great scientific school will contribute their full share to the direction and inspiration of industry and public life.

While, therefore, Sir Cyril clearly does not accept much of Dr. Rowe's argument about research and teaching, his address is not a defence of either trivial research or inferior teaching. Rather he calls for teaching of the highest quality, as well as for much independent and critical thinking about methods as well as the content of courses. It may well be that some administrative changes will be needed before ideas such as those outlined by Sir Cyril Hinshelwood and Sir Mark Oliphant are acceptable; further, some changes in the relations between the universities and the schools will be necessary. The changes, however, are not of the kind which Dr. Rowe suggests, and will require much more constructive thought before their shape can be determined. This is one further subject to which attention will no doubt be given when the promised inquiry into higher education is launched; meanwhile, Sir Cyril Hinshelwood and Sir Mark Oliphant have indicated some lines for further thinking and inquiry as well as for profitable experiment.

PAULING'S CHEMICAL BOND

The Nature of the Chemical Bond and the Structure of Molecules and Crystals

An Introduction to Modern Structural Chemistry. By Prof. Linus Pauling. Third edition. (The George Fisher Baker Non-resident Lectureship in Chemistry at Cornell University.) Pp. xx+644. (Ithaca, New York: Cornell University Press; London: Oxford University Press, 1960.) 60s. net.

WHEN the first edition of this book was published in 1939 it was immediately recognized as a classic; for many chemists it became a sort of professional bible. I recall clearly my own sense of breathless astonishment at the scale, the self-confidence, the brilliance and certainty of the author's ideas. For the first time the theory of the chemical bond became a unified and homogeneous, sustained theme. Prof. Pauling rightly received his Nobel Prize for being so largely responsible for this.

Now the third edition is in our hands. It is larger, though many of the older pages survive with little alteration. Inevitably some changes were needed in such matters as bond-energies and bond-lengths, to allow for better experimental information now available. But the author has added new material, notably on his order-length relation for resonating bonds, on his theory of metals (here he has carried almost alone the weight of battle against the physicists), and on the new and interesting electron-deficient compounds (of which the bridged molecule of diborane is the simplest example). We should be grateful for all this, particularly in the discussion of metallic bonding and the metallic radii of atoms. Some of us may even be tempted to smile quietly at the new pages devoted to the defence of resonance as being no more 'idealistic' than any other theory of chemical bonding. This is a barbed shaft, aimed in a particular direction; and it hits its mark.

There is no doubt but that this new edition will carry the influence of Linus Pauling a stage further. Yet it is impossible—after twenty-two years use of the earlier edition—not to recognize that the book's very success is a pointer to at least one present weakness. For in order to achieve so wonderful a unification of chemistry, Prof. Pauling was almost forced to adopt just one line of description. This is the description first introduced by Heitler and London in 1927, and extended (very largely) by Pauling himself. We call it the familiar valence-bond, or electron-pair, theory. But what he has not done is to provide a really good critique of this theory, or any sufficiently generous reference to the theory's chief rival, the molecular-orbital theory of Hund, Mulliken and Lennard-Jones.

Let me illustrate both of these points. In the first place, very few people who read the pages here devoted to the relation between the dipole moment of a diatomic molecule and the description of its electronic structure in terms of covalent-ionic resonance will gain any idea of the extreme delicacy which attends any calculation or interpretation of molecular dipole moments. An example of the second criticism occurs in the discussion of the new molecular 'sandwich' molecules such as ferrocene. If the valence bond method is adopted, there are no less than 560 structures to be considered. In nickelocene there are 4,100. Pauling starts his account of this latter compound: "With the assumption that the 4,100 structures have equal weight. . . ". Some reference really ought to have been made to the fact that in systems like this, and in a large part of the chemistry of inorganic complexes, the molecular-orbital description is vastly simpler, devoid of sweeping assumptions and easier to visualize. There will be many others as well as myself who regret that ligand field theory is dismissed in just over one page.

Yet these limitations in the book are almost inevitable if the author's theme is to remain as grand and monolithic as the structure of the book demands. If the reader can be kept occasionally reminded that there are alternative ways of thinking about the nature of the chemical bond, he can turn to this new "Nature of the Chemical Bond" and experience all the exhilaration and thrill that come from being in the presence of a master of the art of exposition, a man with an immense knowledge of chemistry and passion for it; and whose influence will remain for so long as wave-mechanical ideas continue to provide our best tool for getting to the heart of the structure of molecules and crystals. C. A. COULSON

LEUKÆMIA

Leukæmia

Research and Clinical Practice. By F. G. J. Hayhoe. Pp. viii+335+28 plates. (London: J. and A. Churchill, Ltd., 1960.) 80s. net.

DR. HAYHOE is to be congratulated. His review of one of the widest and most varied fields of practical and experimental medicine is not only remarkably comprehensive but also readable. Each chapter covers a logically delineated region. Difficult questions are not avoided, but a reader

fairly new to the subject will not feel choked by incompatible observations or rival theories. Even when discussing subjects to which he has made important original contributions, such as the cytochemistry of the leukæmic cell, Dr. Hayhoe has maintained a critical detachment. The chapter on this subject is one of the most valuable in the book.

There are many other excellent chapters. Outstanding are the critical reviews (Chapter 3) of existing statistical evidence for an increase in incidence of leukæmia in recent years, and for differences in incidence between different countries and races, and the clear account (Chapter 7) of the confusing subject of antigenicity and immunology of the leukæmic cell.

Dr. Hayhoe has surveyed the literature issued up to about the end of 1958. In some fields advances since then have been far-reaching, and I think he would probably modify one or two of his statements to-day. For example, he regards the question whether those conditions variously known as 'homologous', 'runt', and 'wasting' disease are due to a graft-antihost or a host-antigraft reaction as still open (pp. 52-54, and 153). Recent evidence (summarized, for example, in an article by Kaplan and Smithers[1]) leaves little doubt that they are caused by the former.

The statement on p. 61 that "In all this work on leukæmia transmission by filterable agents the type of leukæmia involved has been lymphocytic" is based, I think, on a misconception of the nature of the tumour-filtrate-induced leukæmia of Graffi[2]. Dr. Hayhoe refers to it (p. 60) as lymphocytic, but Graffi and his colleagues describe it as a chloroleukæmia of myeloid type, and others who have examined his material agree. The other possible exception to Dr. Hayhoe's rule, the condition described by Friend[3], is a doubtful case: it is now considered to be of mixed origin[4].

An interesting recent development in this field is reported by Gross[5]. He has observed the induction of myeloid leukæmia, by a filterable agent which usually produces lymphoid leukæmia, in mice protected against the latter disease by thymectomy. It is now clear that leukæmias of myeloid, lymphatic, and perhaps other types may all be transmissible by cell-free agents.

The question of the relation between the so-called 'polyoma' agent (which produces both sarcomata and carcinomata in various organs of mice and other animals inoculated soon after birth) and the leukæmogenic agent, with which it is often associated, has also been considerably clarified since the book was written. The former is a typical virus, producing cytopathic effects in tissue culture, and agglutinating red cells, and differs in many ways from the latter, which is so far recognizable with certainty only by its leukæmogenic effects. As might be expected in such a fertile field of research, other important advances have been made since Dr. Hayhoe closed his survey. For example, analysis of the role of the thymus in filterable agent-induced leukæmia[6–8], and the isolation of a filterable leukæmogenic agent from X-ray-induced leukæmia[9,10] promise exciting future developments in our understanding of this dreaded disease. To these and other investigations Dr. Hayhoe has provided an excellent introduction.

The clinical sections of this book are concise and lucid, and his account of the depressing failures of therapy is relieved by painstaking evaluation of those measures which can reduce distress and occasionally prolong life. The beautiful plates, both coloured drawings and black-and-white photomicrographs, are well chosen, and the excellent plan is adopted of introducing the same plates in several groupings to illustrate different aspects of the conditions described.

The book will be found on the shelves of physicians and laboratory workers for many years to come, and one, at least, of the latter hopes that it will help each group to understand what the other is doing.

M. H. Salaman

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FORAGE CONSERVATION

The Conservation of Grass and Forage Crops

By Prof. Stephen J. Watson and Dr. Michael J. Nash. Second enlarged edition. Pp. xiv + 758. (Edinburgh and London: Oliver and Boyd, Ltd., 1960.) 84*s*. net.

GRASSLAND and other forages grown for animal feeding provide the basis of livestock industries throughout the world and within most farming systems that involve livestock. Under British conditions, grassland herbage as grazed by the ruminant animal provides the cheapest and in many ways the best method of feeding cattle and sheep. However skilful the management of grass, conservation of the summer surplus will always be required to maintain animals during winter. Since 1940 the British farmer has learnt how to extend his annual grazing season, and this has coincided with a greatly increased level of animal production. Thus, although the winter feeding period is now considerably shorter than a quarter century ago, the need for conservation of grass and other forages is as important and as vital as ever it was. Indeed the need for preserving grass when its quality is at maximum was never more vital to our livestock husbandry systems.

It is therefore a most opportune time for the publication of this book by Prof. S. J. Watson and Dr. M. J. Nash. The new volume offers an enlarged and re-written edition of Prof. Watson's earlier edition published in 1939. Since that time the volume of additional work dealing with fodder conservation has been staggering; but this has served to confirm and to clarify many of the underlying principles of conservation which were broadly known two decades ago. In the earlier edition Prof. Watson had made what was perhaps the first widely embracing attempt to review the experimental work of pre-war days; now he and his collaborator have skilfully collated the work on fodder conservation since that time. This second edition is an authoritative compilation of a massive amount of experimental and practical evidence from all over the world. As such it is bound to be accepted as a book of reference and is likely to remain a classic for a very long time to come.

The traditional methods of fodder conservation as hay or silage have notorious defects: the unreliability of hay in most climates and the serious loss of nutrients normal to both hay and silage as conserved to-day. There has been much controversy as to the relative merits of hay and silage; the authors point out that hay and silage are not competitive but are complementary foodstuffs. The staggering feature which every practical farmer as well as technician should note and ponder on is the huge loss of nutrients that takes place annually during the processes of fodder conservation. The authors show that losses of starch equivalent normal in haymaking under reasonably good conditions are on average as high as 42 per cent; this level is only reduced to 35 per cent by barn drying and the use of other modern techniques.

The losses in silage-making are also high; for example, the summary of data from a large number of experiments shows that while losses in dry matter may be no more than one-sixth, the loss in starch equivalent is more than one-fourth while the losses in digestible true protein exceed one-half. These data are from experimental records; one may properly surmise that the losses encountered during silage preservation on the average farm are greatly in excess of the figures quoted from carefully conducted experiments. The most striking feature in most of our conservation practices is the astounding loss of nutrients which appears to occur. This fact surely adds emphasis to the plea made by the authors (in their preface) for a more complete study than hitherto of the fundamental chemical and biological changes which occur during the process of fodder conservation.

The book is well produced and well edited. The subject index is reasonably adequate and there is a most valuable index of authors occupying some fifty pages towards the end of the book. This is a book of reference which should find a place in every library as well as on the private bookshelf of all those interested in feeding farm animals.

WILLIAM DAVIES

SPACE SCIENCE

Introduction to Space

By Dr. Lee A. DuBridge. Pp. xii+93. (New York: Columbia University Press; London: Oxford University Press, 1960.) 20*s*. net.

THE George B. Pegram lectureship is awarded annually to an individual who has made outstanding contributions to modern society. The first recipient was Dr. L. A. DuBridge, president of the California Institute of Technology, who gave four lectures on space science, now published as a book.

The first lecture, entitled "Attaining a Space Orbit", consists of a brief history of American rocket development, followed by a discussion of the technological difficulties involved in placing a satellite in orbit. It includes a simple description of the basic parameters which characterize a selected orbit, and this lecture is perhaps the best of the four.

The second lecture discusses the value of satellites and rockets as observing stations, together with the problems encountered in conveying the results of the observations back to the ground. The author remarks on the difficulty of recovering packages from satellites and suggests we should let future generations struggle with the problem, a pessimism confounded by events shortly after the book was sent to press. The lecture contains a rapid survey of phenomena occurring in space which satellite observations should help to clarify, but it is little more than a catalogue, too superficial for the scientist and too technical for the non-scientist.

The last two lectures are devoted to, respectively, the solar system and the universe, each taking about twenty pages. The lecture on the solar system lists some facts about the Moon and the planets (though Saturn is dismissed with the remark that it will bear a closer look) and mentions some of the problems associated with landing on the Moon, Mars and Venus. The lecture on the universe is more interesting, and the author succeeds in compressing a large amount of material into a few pages without lapsing into unintelligibility.

The book is intended to provide a broad picture for the non-scientist of the use of rockets and satellites in adding to our understanding of the physics of space. As such it is successful within the limitations imposed by its length of ninety pages, and it can be recommended to all those prepared to tolerate occasional maltreatment of the English language. The book contains some good photographs of the major planets.

A. DALGARNO

THE REAL MATTER OF NUCLEAR ENERGY

Metallurgy and Fuels

Vol. 2. Edited by H. M. Finniston and J. P. Howe. (Progress in Nuclear Energy, Series 5). Pp. ix+653. (London and New York: Pergamon Press, 1959.) 147*s*. net.

ANY attempt to collect into one source and to review a large part of the flood of publications on nuclear energy must now arouse gratitude, and unless it is very badly done it must be valuable to workers now overwhelmed by the enormous amount of literature on this subject. "Progress in Nuclear Energy" is a series, now well established, of reviews in volumes each covering a particular field. Volume 2 of "Metallurgy and Fuels" surveys in forty-one chapters work done between the first International Conference on the Peaceful Uses of Atomic Energy at Geneva in 1955 and the end of 1957, on basic materials of nuclear energy and on problems in physical metallurgy arising in the field. Materials considered are uranium, thorium, magnesium and its alloys, plutonium, zirconium, beryllium, control materials, and uranium and thorium oxides. Work on several types of fuel-element is reported. Subjects in physical metallurgy include constitutional work on alloys of nuclear fuel metals; transformation kinetics in uranium alloys and effects of irradiation on matter.

The standard of the reviews in this large volume of 631 pages is generally very high, although one or two fall rather far below the others and the value of publishing these may be doubted. They vary very much in length, in the breadth of field covered and in the detail of reporting: it is not clear whether there was editorial policy on this last point, or whether it was left to authors to choose how each would handle his subject. Weber reviews

recent progress in the fabrication and application of dispersion fuel-elements in a long (62 pages) and very well-documented paper, the value and importance of which is at once made clear by the list of 82 publications considered. Grainger covers the important work on elements for gas-cooled reactors with authority in a short but very informative and careful chapter. Typical of shorter chapters on very specialized subjects are Corzine's three-page report on the induction melting of thorium and the chapter by Antill, Butler and Barnes on the electrolytic purification of uranium: each of these appears to be based on only one or two publications and also on material not previously published. The wisdom of publishing material for the first time, if indeed this is occurring, would seem to be open to question. Kroll's statement on the production of uranium billets in Belgium from African ore is interesting, but appears without any references to reports containing details of the work he presents so tersely.

Three very useful chapters present in a non-critical way alloy constitutional diagrams of systems containing plutonium, uranium or thorium. Other reviews tend clearly to present the author's opinion on matters not yet settled. This is, perhaps, inevitable and to those who know the authors it may be valuable, but it might be helpful to have editorial guidance as to the policy followed in some cases.

Work in some of the fields reviewed has been continued. The Second International Conference on the Peaceful Uses of Atomic Energy in 1958 led to the publication of an enormous amount of work on nuclear materials which, it is promised, will be reported in another volume in this "Progress in Nuclear Energy" series. It is indeed valuable that the volume under review collects in one book the scattered information available just before so much new material was published as one event.

It is a pity that the price of this volume (£7 7*s*.) is high enough to discourage many workers in the field from buying their own copies. In a collection of quick surveys of the position in parts of the field this might not be very important, but many authoritative parts of this book would be valuable for frequent reference.

It is to be hoped that further volumes in this series on "Metallurgy and Fuels" will appear regularly and that the high standard of the present volume will be maintained.

G. A. Geach

CONGESTION IN TELEPHONE SYSTEMS

Introduction to Congestion Theory in Telephone Systems

By R. Syski. Chapter 2 by N. H. G. Morris. Pp. xvi + 742 + 14 plates. (Edinburgh and London: Oliver and Boyd, Ltd., 1960. Published for Automatic Telephone and Electric Company Limited.) 105*s*. net.

Most engineers and many mathematicians remember with respect the book, "Probability and its Engineering Uses", by T. C. Fry, published in 1928. This pioneering text paved the way for a wide appreciation, in the practical world of technology, of the concepts of mathematical probability and its applications. Now, after thirty years, a worthy successor to Fry's book has appeared. It will undoubtedly become the standard reference for telephone engineers who have occasion to study congestion in the treatment of design problems. But it will become more than this. The book by Mr. Syski, while it contains several chapters dealing specifically with telephone matters, is the first really comprehensive account in book form of the theory of queueing. It is a well-integrated text and includes an account of practically all the ideas which have proved capable of mathematical development in this field during recent decades. Thus, it is likely to become something of a standard work on queueing theory for teachers and students in the field of operations research and, more generally, in institutions where the applied mathematics courses include the topics of probability and stochastic processes.

After an introductory chapter, and one discussing the constructional details of telephone systems, there is a chapter of about fifty pages on probability theory. The latter is well written and may be properly understood by mathematicians. But there seems to be some doubt as to whether the telephone engineer will make much of the rather abstract mathematical formulation. Sample spaces and an introduction to operations with sets may be all right. But the introduction of measure and of Borel spaces will probably prove to be difficult for the engineer unless he has pursued mathematics to an unusual degree. There are nice accounts of random variables, distribution functions and conditional probability, and a feature of the exposition is the wealth of illustrative examples. The account of stochastic processes again seems rather 'highbrow' for the engineer.

The next two chapters are concerned with traffic characteristics and loss systems. Included are introductions to renewal processes generally, and the birth and death process. Waiting systems are treated in a chapter of about one hundred pages and both single- and many-channel systems are studied. These include the systems $M/M/r$, $M/D/r$, $M/G/r$, $GI/M/r$ and $GI/G/r$. Congestion in systems with limited availability is studied in the next chapter, and then there is a chapter on link systems. Some of the most interesting results of recent research are discussed in the chapter on special systems. These results relate to the busy periods, various forms of priority and servicing, early departures, finite queues and queues in series, and to special problems such as the clustering effect, intensity fluctuations, and hunting problems. This chapter should be of special interest to the student starting on research in the theory of queueing. The last chapter deals with some problems special to telephone exchanges.

It is interesting to compare the flavour or atmosphere of this book with that of the earlier book by Fry. Both are heavily mathematical. But the remarkable difference is in the degree of abstraction. Syski has certainly demonstrated that what is called 'abstraction' in mathematics has invaded parts of the subject which are of the greatest application. There is no justification for pursuing mathematical abstraction for its own sake. But, on the other hand, this feature of modern mathematics has become an essential part of the tools needed in various applied fields. We cannot avoid it; and, one corollary appears to be the necessity for training engineers to a higher level of abstraction than traditional courses contemplate.

L. S. Goddard

The Popular Handbook of Rarer British Birds

By P. A. D. Hollom. Pp. xiv+133+40 plates. (London: H. F. and G. Witherby, Ltd., 1960.) 37*s*. 6*d*.

THIS useful book supplements the "Popular Handbook of British Birds" (1952), edited by Mr. P. A. D. Hollom, which excluded species that had been recorded in the British Isles on less than a dozen occasions. Both works are based on the five volumes of the authoritative "Handbook of British Birds" (1938-41) by H. F. Witherby and others, and although much detail is necessarily omitted they include information of more recent date. The latter feature is especially noticeable in this instance, as accounts and illustrations are given of some thirty species which were not included in the original work at all, having been added to the British list in the intervening two decades.

Many of the new birds are vagrants from America, others from Asia or from southern Europe. Some of them represent groups which found no place in earlier books on British birds—frigate-birds, vireos, New World warblers, New World orioles, tanagers and American sparrows. Several of the newcomers have already been reported more than once, and there are further records of others previously on the list, thanks to the activity of our coastal bird-observatories and the expertise of our field workers. Many of the species are thus likely to come to notice again, and a hand-book covering this aspect of British ornithology is very welcome. The information given for each species is in convenient form, covering identification in some detail and with briefer notes on habits, British occurrences and general distribution. The colour plates not available from the original work are by D. M. Reid-Henry and Peter Scott. LANDSBOROUGH THOMSON

Elementary Titrimetric Analysis

By Dr. A. M. G. Macdonald. Pp. viii+133. (London: Butterworths Scientific Publications, 1960.) 12*s*. 6*d*.

THIS book deals exclusively with titrimetric procedures, and although it has been written primarily for students in schools and junior technical colleges, it also deals in an informative manner with the application of redox titrations and the use of complexanes in titrimetry, and these chapters would be well worth the attention of somewhat more advanced students.

The chemical purist might quarrel with Dr. Macdonald's definition of the gram equivalent weight of the acid as the weight which "furnishes one gram of hydrogen ion", and might prefer the more exact definition which would relate to '1·008 gm. of hydrogen ion'. Indeed, the 1957 "Table of Atomic Weights" given at the end of the book quotes atomic weights to three decimal places, and the student might often ponder as to why the gram equivalent weight of sulphuric acid is given as 49 and not as 49·041.

The reviewer also feels that some chapters could have been presented in a clearer manner to the student if diagrammatic illustrations were used; for example, in the chapter on oxidation potentials, a sketch of a redox electrode with salt bridge to a calomel electrode would have been most informative.

These points are, however, minor criticisms, for the book is well balanced and introduces the student gradually to the more difficult exercises of volumetric quantitative analysis. The general descriptions of indicator applications, hydrogen ion concentration, etc., are considered to be completely adequate for the average student, and the theoretical implications have been clearly and concisely described.

In this context the book will prove valuable not only to the student, but also to the teacher of chemistry who has to present the subject of titrimetric analysis to his classes in a manner which makes the theoretical implications easily comprehensible, and the practical exercises suggested are well balanced and cover a wide and useful range of analytical procedures. D. T. LEWIS

Life's Long Journey

By Kenneth Walker. Pp. 191. (London: Victor Gollancz, Ltd., 1960.) 21*s*. net.

THE aim of Dr. Kenneth Walker's latest book is to show that mechanistic views of life are long outdated, and that the universe is essentially spiritual in essence. To arrive at his ultimate conclusion that "it is to religion . . . that man will have to turn for help if he is to evolve any further", Walker roundly assails all neo-Darwinians as well as those who condition our minds by too much science.

The book is unsatisfactory in many respects. Few people will accept Walker's disarming prefatory note that his amateur acquaintance with biology makes him in some way more fitted to interpret its main hypothesis than those who have studied more deeply. His interpretations of Darwin's theory of natural selection do not always represent the views of the progenitor. Dogmatic reiteration of the purposefulness of life does not necessarily make life more purposeful, and is scarcely in keeping with a scientific mode of thinking. The mystical references to Eastern religions as sources of revelation to those to whom the mysteries are vouchsafed are unlikely to console those who profess Western faiths, and who read that "we live in a post-Christian age and an age in which economic man has been allowed to usurp the rights of the whole man". Walker's wish was that this book would help many to look again at the meaning of life; it is unfortunate that its appeal will, for the most, be to those whose minds are already made up. T. H. HAWKINS

The Lichen Flora of the United States

By Bruce Fink. Second printing. Pp. xii+426+47 plates. (Ann Arbor: University of Michigan Press; London: Angus and Robertson, Ltd., 1960.) 12.50 dollars; 50*s*.

THIS is an exact copy of the original edition published in 1935, even to such obvious errors as the transposition of captions on Plate 42. Unfortunately, the erratum slip issued with the former volume has not been reproduced. It seems a pity the opportunity was not taken to rewrite the accounts of such genera as have been revised in North America during the past quarter century, but to do so would doubtless have led to a somewhat uneven treatment of the flora as a whole. Naturalists in the United States will be glad to have this convenient basic summary of their lichen flora once more available. R. W. G. DENNIS

CALENDAR OF CENTENARIES, 1961

JANUARY

4 *Hales, Stephen* (1677–1761), English clergyman who carried out fundamental researches in plant and animal physiology and was awarded the Copley Medal of the Royal Society in 1739.

8 *Clegg, Samuel* (1781–1861), English gas engineer, pioneer in gas lighting.

12 *Baldwin, James Mark* (1861–1934), American philosopher and psychologist.

17 *Hall, Sir James* (1761–1832), Scottish geologist who carried out laboratory experiments to investigate and illustrate geological phenomena.

18 *Goldschmidt, Hans* (1861–1923), German chemist whose name is associated with the thermit process for the reduction of metallic oxides.

22 *Bacon, Francis* (1561–1626), English philosopher whose works include the "New Atlantis" in which is described a model college for the experimental study of Nature.

22 *Tiedemann, Friedrich* (1781–1861), German physiologist and anatomist.

FEBRUARY

15 *Whitehead, Alfred North* (1861–1947), English mathematician and philosopher.

15 *Guillaume, Charles Edouard* (1861–1938), Swiss physicist, awarded the Nobel Prize for Physics in 1920 for his work on nickel-steel alloys.

24 *Santorio, Santorio* (1561–1636), Italian physician and physiologist, author of the medical classic, "Ars de Statica Medicina" (1614).

APRIL

6 *Giesecke, Karl Ludwig* (1761–1833), German mineralogist who travelled extensively in Greenland and located the unique occurrence of cryolite there.

8 *Peurbach, Georg* (1423–61), professor of astronomy in Vienna who revived observational astronomy in western Europe.

MAY

3 *Vallisnieri, Antonio* (1661–1730), Italian physician and naturalist who made valuable observations on fossils and the origin of springs.

13 *Fitton, William Henry* (1780–1861), Irish physician and geologist, author of an important memoir on the strata below the Chalk in south-east England.

14 *Simpson, Thomas* (1710–61), English mathematician, author of a number of mathematical books.

16 *Henslow, John Stevens* (1796–1861), professor first of mineralogy, then of botany, at Cambridge, who nominated Charles Darwin as naturalist for the voyage of the *Beagle*.

JUNE

7 *Rennie, John* (1761–1821), Scottish civil engineer, constructor of canals, bridges and harbours.

18 *Hodgkinson, Eaton* (1789–1861), English civil engineer, noted for his researches on the strength of materials.

24 *Gregory, David* (1661–1708), Scottish mathematician, who, as professor of mathematics in Edinburgh, gave the first public lectures on the Newtonian theory.

29 *Mayo, William James* (1861–1939), American surgeon who, jointly with his father and brother, founded the Mayo Clinic, Rochester, Minnesota.

30 *Hopkins, Sir Frederick Gowland* (1861–1947), English biochemist who received (jointly with C. Eijkman) the Nobel Prize for Medicine and Physiology in 1920.

JULY

8 *Thomson, Sir John Arthur* (1861–1933), Scottish biologist, author of many technical and popular works.

AUGUST

8 *Bateson, William* (1861–1926), English biologist who carried out an extensive investigation of the laws of variation and heredity.

10 *Wright, Sir Almroth Edward* (1861–1947), English bacteriologist and pioneer of vaccine therapy.

SEPTEMBER

8 *Belidor, Bernard Forest de* (1693–1761), French military engineer, author of works on engineering and hydraulics.

17 *Bose, Georg Mathias* (1710–61), German natural philosopher who carried out many experiments with static electricity, some of which he described in a poem, "Die Elektricität" (1744).

19 (or 9) *Musschenbroek, Pieter van* (1692–1761), Dutch physicist who invented a pyrometer and who was concerned with the discovery of the Leyden jar.

24 *Pitiscus, Bartholomaeus* (1561–1613), German mathematician who prepared an early work on trigonometry.

OCTOBER

13 *Cubitt, Sir William* (1785–1861), English civil engineer, responsible for the construction of important docks and canals.

NOVEMBER

7 *Sherrington, Sir Charles Scott* (1861–1952), English physiologist, awarded the Nobel Prize for Medicine and Physiology in 1932 (jointly with E. D. Adrian) for researches on the nervous system.

30 *Dollond, John* (1706–61), English optician, who received the Copley Medal of the Royal Society for his work on achromatic lenses.

30 *Tennant, Smithson* (1761–1815), English chemist, discoverer of osmium and iridium.

DECEMBER

17 *Kennelly, Arthur Edwin* (1861–1939), American physicist who independently predicted the existence of the Heaviside layer.

24 *Pons, Jean Louis* (1761–1831), French astronomer who discovered more than thirty comets.

25 *Gregor, William* (1761–1817), English chemist and mineralogist, discoverer of titanium.

INTERNATIONAL GEOPHYSICAL CALENDAR FOR 1961

THE accompanying International Geophysical Calendar 1961 indicates some special days and intervals for special attention for geophysical experiments and analysis. It serves to encourage world-wide co-ordination of observation or analysis of those geophysical phenomena which vary significantly during the course of a year. These phenomena are mainly in the scientific disciplines dealing with the Earth's atmosphere. In some experiments, such as the routine measuring of variations of the Earth's magnetic field, the observing and analysis programmes at observatories are carried out at a uniform level throughout the year; in these cases the Calendar is not needed. However, in many other experiments (for example, rocket experiments), it is not practical or meaningful to carry out the same programme on each and every day. Here the Calendar can provide a useful mechanism for co-ordination. Experimenters will know that their colleagues in other laboratories and in other disciplines will tend also to carry out experiments on the days or intervals marked on the Calendar. In this way, results of experiments may be more easily and usefully compared.

In some scientific fields, international scientific organizations have made specific recommendations for programmes to be done on days or intervals marked on the Calendar. In others, the arrangements are informal or self-evident. Some examples are given below, along with the criteria for selection of dates.

Copies of the Calendar can be obtained from the Secretary-General, U.R.S.I., 7 Place Emile Danco, Brussels 18.

Regular World Days

These are three consecutive days each month. They always come in the middle or just after the middle of the month, and include where possible the times of equinox and solstice. They come in the middle of the week—Tuesday, Wednesday and Thursday. The groups of Regular World Days are evenly spaced through the year so far as it is practical. They include wherever possible days of solar eclipse and meteor showers. One Regular World Day each month (always Wednesday) is designated the Regular World Day of highest priority.

The Regular World Days are intended for experiments or observational programmes or analysis programmes which as a practical matter can be done only about 10 per cent of the time and should be spaced through the year. Further, it is suggested that whenever there are no special reasons for selecting some other days, the Regular World Days be used for unusual or special experiments. This applies perhaps particularly to scientific fields in atmospheric geophysics, including aspects of cosmic rays, meteorology, airglow, ionosphere, geomagnetism, aeronomy. Examples in ionospheric physics are: oblique incidence pulse transmission and reception; absorption measurements by pulse reflexion technique; extended observing schedule for whistlers and very low-frequency emissions; vertical-sounding observing schedule faster than normal; more detailed reduction of vertical-sounding ionograms by f-plot, h'-plot, etc.; hourly reduction from ionograms of F-region true height parameters hc and fc.

The Regular World Days with highest priority are for work which can be undertaken for only one day each month. All the foregoing examples apply if the rate of three days per month is not necessary or proves to be too heavy. A specific example is the recommended programme for 1959 and onwards of exchange of copies of original ionograms in ionospheric vertical sounding work, made by the International Scientific Radio Union–International Geophysical Year (URSI–AGI) Committee; this recommends that ionograms for the highest priority Regular World Day each month (and also one disturbed period each year) be sent to World Data Centres for interchange.

Regular World Intervals

These are ten consecutive days in each quarter year, selected to include the three Regular World Days of the month and also the times of the equinox or solstice. If possible, they include days of solar eclipses and meteor showers. The selectors have also tried to avoid week-end days and in addition holidays which are widely observed.

The Regular World Intervals are intended for experiments which for practical reasons cannot be carried on continuously, but for which statistics of seasonal variations are especially needed. Ionospheric drift and high-atmosphere wind measurements are two examples. Schedules for interchange of sample detailed data in several disciplines have made use of the Regular World Intervals. In some network observational programmes, both the Regular World Intervals and the Regular World Days are used, in order to get the variations throughout the year but with improved statistics at the equinoxes and solstices.

World Meteorological Intervals

The World Meteorological Intervals are ten consecutive days each quarter year, but displaced one month from the equinoxes and solstices. They are intended to cover the times of marked seasonal change in certain meteorological phenomena which tend to come about a month after the equinoxes and solstices. They have been chosen through the World Meteorological Organization and the Committee on Space Research of the International Council of Scientific Unions as the period from the 16th to the 25th of January, April, July and October, with January and October designated by the Committee on Space Research as the more important ones.

The World Meteorological Intervals now are primarily periods for carrying out synoptic meteorological rocket programmes, with stations obtaining atmospheric profiles up to 50 km. or more, at least once daily during the ten-day intervals. These Intervals have also been used during and since the International Geographical Year for balloon sounding programmes either with special instruments or launchings to unusually high balloon altitudes.

International Geophysical Calendar 1961

Issued November 1960 by the International World Day Service under the auspices of the International Scientific Radio Union

1961 JANUARY 1961

S	M	T	W	T	F	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	(17)	(18)	(19)	20	21
*22	23	24	25	26	27	28
29	30	31				

1961 FEBRUARY 1961

S	M	T	W	T	F	S
			1	2	3	4
5	6	7	8	9	10	11
(12	13	(14)	[15]	(16)	17	18)†
19	20	21	22	23	24	25
26	27	28				

1961 MARCH 1961

S	M	T	W	T	F	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	(21)	(22)	(23)	24	25
26	27	28	29	30	31	

1961 APRIL 1961

S	M	T	W	T	F	S
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	(18)	(19)	(20)	21	22
23	24	25	26	27	28	29
30						

1961 MAY 1961

S	M	T	W	T	F	S
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	(16)	(17)	(18)	19	20
21	22	23	24	25	26	27
28	29	30	31			

1961 JUNE 1961

S	M	T	W	T	F	S
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	(20)	(21)	(22)	23	24
25	26	27	28	29	30	

1961 JULY 1961

S	M	T	W	T	F	S
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
(16	17	(18)	(19)	(20)	21	22)
23	24	25	26	27	28	29
30	31					

1961 AUGUST 1961

S	M	T	W	T	F	S
		1	2	3	4	5
6	7	8	9	10	[11]	12
13	14	(15)	(16)	(17)	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

1961 SEPTEMBER 1961

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	(19)	(20)	(21)	22	23
24	25	26	27	28	29	30

1961 OCTOBER 1961

S	M	T	W	T	F	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	(17)	(18)	(19)	20	21
*22	23	24	25	26	27	28
29	30	31				

1961 NOVEMBER 1961

S	M	T	W	T	F	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	(14)	(15)	(16)	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

1961 DECEMBER 1961

S	M	T	W	T	F	S
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	(19)	(20)	(21)	22	23
24	25	26	27	28	29	30
31						

1962 JANUARY 1962

S	M	T	W	T	F	S
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	(16)	(17)	(18)	19	20
21	22	23	24	25	26	27
28	29	30	31			

(17) Regular World Day (RWD)

(18) RWD with highest priority

21 Day with unusual meteor shower activity

[15] Day of solar eclipse

[16 17 18 19...] World Meteorological Interval (WMI)

14 15 16 17... Regular World Interval (RWI)

(12 13 14 15...) International Rocket Week (IRW)

Notes : (*) WMI in January and October considered most important

(†) Feb. 15, 1961 : RWD with highest priority

International Rocket Weeks

These have been chosen for 1961 by the Committee on Space Research as (1) February 12–18 and (2) July 16–22. The first includes the time of the total solar eclipse of February 15 and is intended for study of solar effects. The second was selected for study of (northern hemisphere) summer atmospheric structure.

The International Rocket Weeks provide two periods during the year when rocket studies of the atmosphere and of the Sun will be on as nearly a synoptic basis as is possible at this stage of the science and technology. More detailed recommendations by Working Group 2 of the Committee on Space Research (chairman, J. Bartels) appear in the *COSPAR Information Bulletin*.

Other Special Days

The 1961 Calendar marks the days of solar eclipses —February 15 (total) and August 11 (annular). Some special programmes may be expected to be carried out in appropriate parts of the world to study eclipse effects on the Earth's atmosphere. It is especially important that the record of solar activity during and near the times of eclipses be as full as possible. Many observatories interested in solar activity issue specially detailed reports of their observations on eclipse days to assist the interpretation of the geophysical efforts. Ionospheric stations generally increase their observing programmes on eclipse days even if the magnitude of eclipse at their position is small.

Also shown on the 1961 Calendar are days when the activity of meteor showers is unusually high. Geophysicists using meteor techniques often intensify their observing programmes on these days. Attention is also directed to these days in case ionization produced by meteors may account for unusual effects in other geophysical experiments.

Special Intervals not appearing on 1961 Calendar

The International Geophysical Calendar marks only those dates which can be selected a long time in advance, either by general agreement or, in the case of eclipses and meteor showers, by reliable long-term prediction. Periods of great magnetic, auroral and ionospheric disturbance are also of great geophysical interest and world-wide co-ordination of observation is clearly desirable. This is also done under the auspices of the International World Day Service, in close collaboration with the International Scientific Radio Union Central Committee on URSI-grams, in the programme for the immediate designation of 'Geophysical Alerts' and for selection on a current basis of Special World Intervals (SWI). Arrangements for receipt of such information by telegram or radio broadcast can be made, as may be practical, with one of the solar-geophysical Regional Warning Centres, the telegraphic addresses of which are: (Western Hemisphere) AGIWARN WASHINGTON (U.S.A.); (Western Pacific) AGI KOKUBUNJI (Japan); (Eurasia) NIZMIR MOSCOW (U.S.S.R.); (Western Europe) either IONOSPHARE DARMSTADT (GFR) or GENTELABO PARIS (France) or AGI NEDERHORSTDENBERG (Netherlands). The meteorological telecommunications network co-ordinated by the World Meteorological Organization carries such information once daily soon after 1600 U.T. Descriptions of the Geophysical Alerts and Special World Intervals plan can be obtained from these Centres or from the Secretary of the International World Day Service. Many geophysical stations increase their programmes or carry on special experiments during disturbed periods: the Geophysical Alert and Special World Intervals programme serves to co-ordinate this on a world-wide basis and is especially useful for stations not near the auroral zones, where the beginning of a major disturbance may not be immediately apparent from local observations.

The International World Day Service, in close collaboration with the Central Committee on URSI-grams, also fosters arrangements for prompt notification of major solar flare events which have important and sometimes long-lasting geophysical effects. These notifications are also done through the Regional Warning Centres.

Calendar Records

A summary record of significant solar and geophysical events is being prepared as a Calendar Record for the International Geophysical Year period and also for 1959. This work is now under the auspices of the International World Day Service. If these volumes prove to serve a useful purpose, similar Calendar Records may be compiled for 1960 and 1961.

The International World Day Service was established in 1958 by the International Council of Scientific Unions and is administered by the International Scientific Radio Union, 7 Place Emile Danco, Brussels 18, Belgium. Its Steering Committee consists of A. H. Shapley (International Scientific Radio Union), M. Nicolet (International Union of Geodesy and Geophysics), and J. F. Denisse (International Astronomical Union), with R. Coutrez (International Scientific Radio Union) as secretary. It obtains nominal support from the Federation of Astronomical and Geophysical Services of the International Council of Scientific Unions. Mr. Shapley, National Bureau of Standards, Boulder Laboratories, Boulder, Colorado, U.S.A., serves as spokesman for the International World Day Service and its correspondent to other groups of the International Council such as the International Committee of Geophysics and the Committee on Space Research.

The International Geophysical Calendar for 1961 has been drawn up by A. H. Shapley and J. V. Lincoln in consultation with the International Scientific Radio Union, the International Union of Geodesy and Geophysics and the International Astronomical Union, both directly and through the International Committee on Geophysics and the Committee on Space Research. Recommendations also have come from representatives of the World Meteorological Organization and from interested individual scientists. A similar Calendar was issued for 1960 along the lines of the calendars for the International Geophysical Year and the International Geophysical Co-operation 1959 issued under the auspices of the Special Committee of the International Council of Scientific Unions for the International Geophysical Year, and described in the International Geophysical Year Instruction Manual for World Days and Communications, *IGY Annals*, VII (Pergamon Press, 1959).

A. H. SHAPLEY

A NEW METHOD FOR DATING ANCIENT GLASS

By ROBERT H. BRILL and HARRISON P. HOOD

The Corning Museum of Glass, Corning Glass Center, Corning, New York

THE majority of glasses surviving from most historical periods have soda-lime-silica or potash-lime-silica compositions. Glasses with these compositions, similar to some in use to-day, are usually regarded as substances of considerable chemical durability in comparison with many other materials; that is, they are resistant to extensive chemical attack except under unusual or extremely corrosive conditions. Actually, however, even in rather mild chemical environments, glasses of this kind, particularly those having high soda or potash content, are subject to a slow chemical deterioration in the presence of water. The accumulated effect of this slow but persistent hydrolytic attack may be readily seen during a visit to any museum displaying a collection of archæological objects of glass which have been weathered because of burial in soil or exposure to the elements for long periods of time.

Weathering effects on glass appear most often in the form of crusts of decomposition products and show a remarkable variability in appearance resulting from variations in chemical composition and weathering conditions. A number of investigators[1–6], beginning with Brewster in 1863, have made microscope studies of these weathering crusts and have noted that in cross-section the crusts can often be resolved into fine laminar structures. The individual layers of these structures range in thickness from about 0·3μ to perhaps 15μ, and are responsible, through interference phenomena[3], for the striking and colourful iridescence so familiar in archæological specimens of glass.

Most of the work done to date has been largely phenomenological, but it has been suggested that the laminar structures are the result of a mechanism similar to that producing Liesegang rings[6,7]. An alternative explanation, however, may be deduced from the realization that the weathering crusts on archæological objects of glass have been formed over extended periods of time and that the appearance of minute individual layers might be a reflexion of some periodic or cyclical change which was imposed during the long time of exposure. For example, seasonal variations in temperature or alternating periods of rainy and dry seasons might be responsible for the lamination effects. Since such phenomena occur in yearly cycles, the exciting possibility arises of dating archæological specimens of glass with extreme accuracy simply by counting the number of individual layers comprising weathering crusts. This possibility is strengthened by our experiences with the leaching of borosilicate glasses involved in the production of 'Vycor' brand glass. When leaching is carried on under very carefully controlled constant conditions, perfectly clear non-laminar sections an inch in thickness are readily obtained. However, every small change in temperature or concentration of the bath during leaching records the event permanently with a discontinuity of refractive index in the leached specimen.

Table 1

Sample	Date based on archæological evidence	Excavation date	Layers counted	Date calculated for onset of weathering
J-5	Submerged **1781**	1935	150–**156**–170	1765–**1779**–1785
J-4	Buried **1639–1670**	1935	256–**266**–273	1662–**1669**–1670
J-6	Buried *c.* **1660–1675**	1935	261–**271**–286	1649–**1664**–1674
J-2	Submerged *c.* **1600–1640**	1956	295–**310**–320	1636–**1646**–1661
PI-1	Buried **1676** or later	1959	259–**269**–289	1670–**1690**–1700
PR-5	Submerged **1692**	1959	258–**268**–274	1685–**1691**–1701
SA-2	Submerged **1621**	1959	319–**334**–349	1610–**1625**–1640
N-4	Manufactured eighth–tenth century	*c.* 1950	**930** ± 20	A.D. **1020** ± 30
N-9	ninth–thirteenth century	*c.* 1950	**775** ± 20	A.D. **1175** ± 20
N-11	ninth–thirteenth century	*c.* 1950	**810** ± 25	A.D. **1140** ± 25
S-15	Late third–early seventh century	1960	**1582** ± 10	A.D. **378** ± 10

In order to test this hypothesis of 'seasonal growth' and explore the dating possibilities, samples were taken from a number of glass objects which had been submerged or buried for known time-intervals. These samples were mounted in plastic, polished, and observed in cross-section under a microscope. The number of individual layers within complete weathering crusts was counted. Typical results are shown in Table 1.

The values reported in Table 1 are averages computed from several independent counts on replicate mountings along with estimated maximum and minimum values. By subtracting the number of layers counted from the known dates of excavation, dates were obtained representing the years when weathering started. The agreement of the dates calculated and those known from archæological evidence is indeed sufficient to substantiate that, for these samples at least, the decomposition proceeded according to a seasonal schedule.

It is reasonable, therefore, to assume that within the limitations to be mentioned below, it is possible to determine total times of exposure to weathering conditions for other glass objects by this counting technique. The results in Table 1 present a rather strong case for the applicability of the method to the Colonial glasses studied, and the date determined for the Sardis fragment leads one to believe that it should be useful for dating more ancient glasses as well. The precision of ± 10 years (at an estimated 90 per cent confidence-level) for a number of counts on duplicate mountings of this sample emphasizes the potential accuracy of the technique. The case is not quite so convincing, however, for the Nishapur

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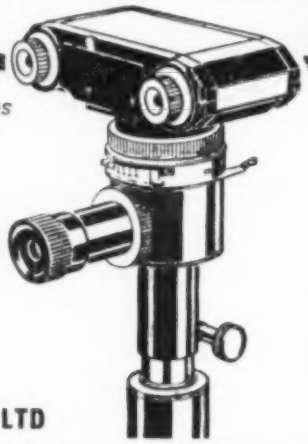

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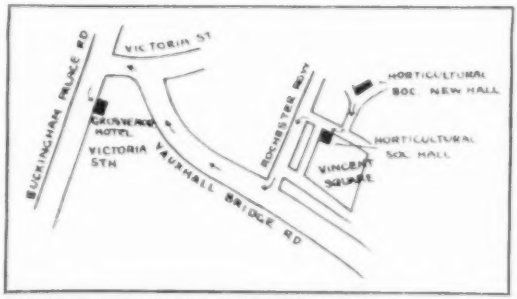

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samples, because they unfortunately cannot be as precisely dated by archæological evidence, and one is, therefore, not certain as to what accuracy has been achieved. There is a need for further work on samples of more ancient origin and such work is being continued at this laboratory.

Although the mechanism of the hydrolytic attack of glass has not been completely elucidated, it almost certainly involves a selective leaching of 'the more soluble ingredients', principally the alkali metal oxides, leaving a hydrated residue of high silica content. On the basis of the results of this investigation, it seems reasonable to postulate that any appreciable and prolonged variation in temperature or availability of water seems to be accompanied by an irreversible change in the structural state of the siliceous residue. This structural change apparently persists even after the original conditions are restored, thus forming a discrete individual layer. Since the layer formed is porous, water may diffuse through from the surroundings during the next 'active' cycle and renew the hydrolytic attack on the body of the remaining glass.

In short, the total extent of weathering must have a complicated dependence on composition, temperature, time and chemical factors such as *p*H ; but the number of individual fine layers appears to depend only on the number of extended temperature cycles or moist – dry cycles experienced, that is, on the number of years of exposure to the elements.

It is not the case, of course, that every sample of archæological glass can be dated satisfactorily by this method. To begin with, the weathering layer must have been preserved intact, a requirement which unfortunately is not met by the majority of fragments available for study. In addition, the conditions of burial must have contained a yearly cyclical factor such as those mentioned above, and the glass itself must be of a composition which confers relative instability towards hydrolytic attack. Among the many objects examined were pieces with crusts of such fragility that they could not be mounted and polished without damaging the laminar structure. This was especially noticeable in Roman glasses. However, with improved techniques of sample preparation, this method of dating may be extended to many more objects. More refined methods of manipulation should also reduce the errors inherent in the counting procedure, for it is on occasion difficult to distinguish individual layers. This is the major source of experimental difficulty encountered and accounts largely for the ranges of uncertainty included in the reported values.

It should be emphasized that this technique does not yield a date of manufacture or use, but rather a date at which the weathering process apparently started. To be useful as a dating technique, it must be further assumed that the weathering process started at the time of burial or submersion. Among the objects included in Table 1, one instance was found where this condition was not fully met. This sample, *J*–4, a fragment of window glass from Jamestown, showed a curious but not uncommon type of decomposition which did not proceed uniformly from the surface of the fragment, but rather proceeded sporadically from randomly located nuclei on the surface, forming cone-shaped intrusions into the body of the glass. These intrusions or 'plugs' have laminar structures which could be counted, but yielded different dates. It is quite evident that all these plugs did not start growing at the same time, but rather that various induction periods lapsed before growth started at some nuclei. The 'oldest' plug found indicated a starting date of 1669. It is most probable that this date represents a date of burial closely coinciding with the date the building was razed. An alternative interpretation might be that the 1669 date refers to a date when the glass was still incorporated as part of a window, thus being exposed to weathering conditions for some years before burial in the soil. Because of the archæological data, the first interpretation seems preferable, although the range of probable error around the 1669 date would make either position tenable.

Perhaps the most important aspect of this investigation is that this method may provide the archæologist with a simple and exceedingly accurate means for dating archæological sites where suitable fragments of glass are found.

Work will be continued at this laboratory on the refinement of experimental procedures for this method, the extension of the method to other archæological materials and on the extraction of climatological data from the layer patterns. When further data have been collected on additional ancient glass samples, the findings will be published in the *Journal of Glass Studies*.

We thank Mr. Paul N. Perrot and Dr. Axel von Saldern, director and curator of The Corning Museum of Glass, for their assistance and encouragement during the course of this work.

Description of Samples

The samples designated with the letter *J* in Table 1 were supplied by Mr. J. Paul Hudson, museum curator at Colonial National Historical Park, Jamestown, Virginia. His descriptions of the samples follow :

J–5. Base from English wine bottle, 1775–81 period. Found inside the hull of a British ship at the bottom of the York River, off shore from Yorktown, Virginia, in 1935. The ship was sunk during the siege of Yorktown in 1781. *J*–4. Small piece of window glass from the First State House at Jamestown, built about 1639, burned or razed about 1670. The fragment was found in damp soil in 1935. It had probably been buried in the soil about 1670. *J*–6. Neck fragment from an English wine bottle of the 1660–75 period. Unearthed in damp soil near a brick foundation of a Jamestown house, 1650–75 period. It appears that the fragment had been buried in the soil from about 1675 until 1935. *J*–2. Neck fragment from a Dutch gin or spirit bottle of the 1600–40 period. Found in water in a Jamestown well in 1956, in association with artefacts of the 1600–40 period.

Pl–1 is a fragment of a small medicine bottle of the sort in common use during the seventeenth century. It was uncovered during the excavation of the site of the Joseph Howland House at Rocky Nook, Kingston, Massachusetts, in 1959. Mr. Harry Schnabel, supervisor of archæology at Plimoth Plantation in Plymouth, Massachusetts, has associated the west cellar of this building, where the fragment was found, with a period of occupation beginning in 1676. *PR*–5 was taken from the neck of a wine bottle recovered during a dredging operation in 1959 at Port Royal. Mr. C. Bernard Lewis, director of

the Institute of Jamaica in Kingston, Jamaica, supplied this bottle, which has been presumed to have been submerged since the earthquake of 1692, when a portion of the city of Port Royal sank below the surface of the sea. *SA*–2, another bottle fragment, was salvaged from a shipwreck off Bermuda by Mr. Mendel Peterson, of the Department of Armed Forces History at the Smithsonian Institution. Mr. Peterson believes that the preponderance of evidence points to this wreck being the remains of the Spanish ship *San Antonio* sunk in 1621, but that a possibility exists that it could be the *Vega* sunk in 1639. *N*–4, *N*–9 and *N*–11 are from the collection of the Corning Museum of Glass. They are Islamic specimens said to have been excavated about 1950 in Nishapur, Iran, at the sites Imam-Zadeh (Ghazi-Abad), Deh-Sheikh and Torb-Abad. The best available estimates for dates of manufacture are those listed in the table. Sample *S*–1 b, is a small lump of glass excavated in 1960 near the House of Bronzes at the site of the ancient city of Sardis in Turkey. Prof. George Hanfmann of the Fogg Museum believes that this building was constructed some time between the late third and early seventh centuries A.D., and that it was destroyed in about A.D. 616.

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IMMUNOLOGICAL TOLERANCE*

By Prof. P. B. MEDAWAR, F.R.S.
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IMMUNOLOGICAL tolerance' may be described as a state of indifference or non-reactivity towards a substance that would normally be expected to excite an immunological response. The term first came to be used in the context of tissue transplantation immunity, that is, of the form of immunity that usually prohibits the grafting of tissues between individuals of different genetic make-up; and it was used to refer only to a non-reactivity caused by exposing animals to antigenic stimuli before they were old enough to undertake an immunological response. For example, if living cells from a mouse of strain *CBA* are injected into an adult mouse of strain *A*, the *CBA* cells will be destroyed by an immunological process, and the *A*-line mouse that received them will destroy any later graft of the same origin with the speed to be expected of an animal immunologically forearmed. But if the *CBA* cells are injected into a fœtal or new-born *A*-line mouse, they are accepted; more than that, the *A*-line mouse, when it grows up, will accept any later graft from a *CBA* donor as if it were its own. I shall begin by using the term immunological tolerance in the rather restricted sense that is illustrated by this experiment, and shall discuss its more general usage later on.

The experiment I have just described[1] can be thought of as an artificial reproduction of an astonishing natural curiosity, the phenomenon of red-cell chimerism in certain dizygotic twins. The blood systems of twin cattle before birth are not sharply distinct from each other, as they are in most other twins; instead, the blood systems make anastomoses with each other, with the effect that the twins can indulge in a prolonged exchange of blood before birth. In 1945, R. D. Owen[2] made the remarkable discovery that most twin cattle are born with, and may retain throughout life, a stable mixture—not necessarily a fifty-fifty mixture—of each other's red cells; it followed, then, that the twin cattle must have exchanged red-cell precursors and not merely red cells in their mutual transfusion before birth. This is the first example of the phenomenon we came to call immunological tolerance; the red cells could not have 'adapted' themselves to their strange environment, because they were in fact identified as native or foreign by those very antigenic properties which, had an adaptation occurred, must necessarily have been transformed. A few years later R. E. Billingham and I[3], with the help of three members of the scientific staff of the Agricultural Research Council, showed that most dizygotic cattle twins would accept skin grafts from each other, and that this mutual tolerance was specific, for skin transplanted from third parties was cast off in the expected fashion. We did not set out with the idea in mind of studying the immunological consequences of the phenomenon described by Owen; on the contrary, we had been goaded by Dr. H. P. Donald into trying to devise a foolproof method of distinguishing monozygotic from dizygotic twins, an enterprise that seemed reasonable enough against the rather thorough background of knowledge we already possessed about the behaviour of skin grafts in experimental animals[4]. It was F. M. Burnet and F. Fenner[5] who first read a general significance into Owen's discovery and who wove it into a general hypothesis of the immunological response which counted the phenomenon of tolerance among its theoretical consequences.

In the outcome, it proved impossible to distinguish between the two kinds of twins by skin grafting; but the causal connexion between Owen's phenomenon and our own was obvious, and we were now confident of our ability to make adult animals accept tissue homografts by reproducing in the laboratory the very state of affairs that had come about by natural accident in twin cattle. Billingham, L. Brent and I eventually succeeded in doing so, and our first report on the matter was published in 1953[1]. In the meantime, M. Hašek[6], working against an entirely different conceptual background, had reproduced Owen's phenomenon in chickens by the ingenious method of making a deliberate synchorial parabiosis between chick embryos in the shell. At hatching the parabionts separated, and from now on they were incapable

* Substance of Nobel Lecture delivered in Stockholm on December 12, 1960.

of making antibodies against each other's red cells, or, as later work showed[7], of rejecting grafts of each other's skin. It is now known that chimerism can occur naturally, though rarely, in twin sheep, and more rarely still in twin human beings[8]; in twin chickens it is probably the general rule. That chimerism should occur in man is clear proof that the principle of tolerance applies to human beings as well as to laboratory animals, and human chimeric twins can accept grafts of each other's skin[8].

Some Properties of the Tolerant State

The main points that emerged from our analysis of the tolerant state were these. In the first place, tolerance must be due to an alteration of the host, not to an antigenic adaptation of the grafted cells, for grafts newly transplanted in adult life have no opportunity to adapt themselves, and the descendants of the cells injected into fœtal or new-born animals can be shown by N. A. Mitchison's methods to retain their antigenic power[10]. Once established, the state of tolerance is systemic; if one part of the body will tolerate a foreign graft, so will another; we found no evidence that a tolerated graft builds up a privileged position for itself within its own lymphatic territory. The stimulus that is responsible for instating tolerance is an antigenic stimulus—one which, had it been applied to older animals, would have caused them to become sensitive or immune. A plural stimulus can induce plural tolerance: the donor will usually contain several important antigens that are lacking in the recipient, and long-lasting tolerance must imply tolerance of them all. The state of tolerance is specific in the sense that it will discriminate between one individual and another, for an animal made tolerant of grafts from one individual will not accept grafts from a second individual unrelated to the first; but it will not discriminate between one tissue and another from the same donor. The injection of leucocytes or lymphoid cells can confer tolerance of skin grafts, for example; and later work has shown that the same is true of grafts of thyroid tissue, ovary, kidney and adrenal gland. These various tissues do indeed differ in their antigenic make-up, but not, apparently, in respect of antigens that play an important part in transplantation immunity. If leucocytes lacked some important antigen present in skin, it is difficult to see how they could confer tolerance of skin; and P. L. Krohn, using more direct and more critical methods, has found it impossible to distinguish between the antigenic make-up, so far as it governs their transplantability, of ovary and skin[11].

Tolerance can be brought promptly and permanently to an end by an experimental device which combines certain principles established by N. A. Mitchison and M. W. Chase. Consider the model experiment described at the beginning of this article, and imagine an *A*-line mouse which is tolerant of *CBA* tissue and which carries a *CBA* skin graft as outward evidence that it is so. The tolerated *CBA* graft can be destroyed within a week by injecting into its host lymphoid cells from *A*-line mice which have reacted on and rejected *CBA* tissues in the expected fashion. A less spectacular but in some ways more informative variant of this 'adoptive immunization' is to inject the tolerant mouse with lymphoid cells from *A*-line mice that have *not* been sensitized beforehand by *CBA* tissues. Here, too, though much more slowly, the tolerant state is brought to an end. The inference we drew from this experiment—and nothing has occurred since to make us question it—was that tolerance is due to a central failure of the mechanism of immunological response and not to some intercession at a peripheral level.

There is one important question about tolerance which the experimental system I have been describing is very ill-equipped to answer: Does the maintenance of the tolerant state depend on the continuing presence of the antigen that provoked it? When living cells are used to procure tolerance they survive into adult life and therefore maintain a chronic antigenic stimulus. But is it necessary that they should do so? So far as transplantation immunity is concerned, no completely confident answer can be given until the antigens that excite it can be extracted in a sufficiently potent form; but with 'tolerance' of foreign proteins and red cells, it does indeed seem that antigen must continue to be present, even though in quantities below the threshold of direct estimation, if a fully non-reactive state is to be maintained[12]. This is one of the most important single pieces of evidence that must be taken into consideration when devising hypotheses to account for tolerance, and it points to the clear distinction that must be drawn between the dosages of antigen necessary on one hand to instate tolerance, and on the other hand to maintain it. Much else is still uncertain—for example, the significance to be attached to the 'partially tolerant' state. Tolerance is not an all-or-nothing phenomenon: every degree of tolerance is to be found, from that which allows a graft to live just perceptibly longer than would be expected of it in a normal animal to that in which the graft is permanently accepted by and incorporated into its host. Is an animal partially tolerant because all its reactive cells are almost completely debilitated, or because, while most of them are completely out of action, a minority retain full possession of their powers?

Tolerance and Runt Disease

It has been the experience of all laboratories that tolerance is most easily procured by injecting lymphoid cells into immature animals. This is not because lymphoid cells are in themselves more strongly antigenic than others—there is evidence that they are not so—but probably because they are distributed throughout the body of the animal into which they are injected. This should make them adept at producing tolerance; an animal can be immune when only a minority of the cells that are competent to do so are reacting immunologically, but cannot be tolerant unless the very great majority of them are not. Unfortunately, the lymphoid cells used to induce tolerance are immunologically qualified to attack the tissues of their host, with consequences that were first revealed by Billingham and Brent[13] and, in a somewhat different form, by M. Simonsen[14]. The injection of foreign adult lymphoid cells into new-born mice of an unrelated strain gives rise to a fatal or chronic illness, 'runt disease', marked by retardation of growth and widespread damage to the host's lymphoid tissue. Its discoverers have proved beyond question that runt disease is immunological in origin. So far as it concerns mice, the clear recognition of runt disease had to await the development of a technique for injecting new-born mice intravenously[14]; until that had been done, there

was every inducement to believe that death or stunting was due to accidental damage caused by injecting cells into mice *in utero*. Runt disease or splenomegaly (one of its earlier symptoms) provides a test of the immunological competence of cells, and lends itself to exact studies of their immunological capabilities; perhaps the most important discovery that can be credited to it is of the presence of an immunologically competent cell in peripheral blood. The aspect of runt disease which concerns us here is its relationship to tolerance. A state of tolerance must obviously abet the onset and probably the progress of runt disease, because if adult lymphoid cells are to attack the tissues of the animal into which they are injected they must live long enough to be able to do so. The frequency with which runt disease was associated with the induction of tolerance gave rise to the suspicion that tolerance might itself be a pathological condition. Might not the adult lymphoid cells used to procure it simply exterminate the developing lymphoid cells of the host and take their place? This cannot be so. Tolerance unaccompanied by any symptom of runt disease is produced by the injection of embryonic cells or by a natural or artificial parabiosis between embryos, and it leads here to a stable chimerism in which native and foreign cells seem to coexist without the one ousting the other. It can be produced, moreover, by adult lymphoid cells which, though antigenically foreign to their hosts, are for simple genetic reasons incapable of attacking them. The experiment described at the beginning is in fact best carried out by injecting, not adult *CBA* lymphoid cells, but adult lymphoid cells from a first generation hybrid between mice of strains *A* and *CBA*. By and large there seems no reason to believe that tolerance can be explained in terms of cellular competition and replacement.

Other Forms of Immunological Non-reactivity

The antigenic substances I have so far had in mind are 'foreign' only in the sense that they derive from other members of their recipients' species. Tolerance of more remotely foreign cellular antigens is more difficult but certainly not impossible to achieve. But even if we confine the concept to the reactions that take place within the compass of a species, it is clear that tolerance can be induced by antigens belonging to more than one chemical class and may extend to more than one modality of response. A tolerant animal fails not only to engage in the 'cellular' type of response we associate with the reaction against homografts of skin; it fails equally to make humoral antibodies—for example, *iso*hæmagglutinins; and the antibodies that fail to make an appearance include those of so-called 'natural' occurrence (for example, human anti-*A* or anti-*B*) as well as those that appear only in response to deliberate immunization. It is not surprising, then, that many authors[16] should have found that a state not yet formally distinguishable from tolerance should be brought about by the injection of purified protein antigens into young animals.

Even in this wider sense tolerance is by no means the only kind of specific immunological non-reactivity[16]. L. D. Felton described and named the phenomenon of 'immunological paralysis' in 1949. Felton showed that adult mice could be immunized and therefore protected against otherwise lethal doses of living pneumococci by the injection of 0·5 μgm. of a pneumococcal polysaccharide of the appropriate antigenic type. But, so far from conferring resistance, the injection of larger doses (500 μgm., for example) abolished it, for the mice became vulnerable to pneumococcal infection and could now no longer be protected against it by an injection of the smaller dose. An analogous phenomenon was discovered by F. J. Dixon and P. H. Maurer when they showed that large doses of soluble protein antigens failed to excite a response from adult rabbits. The foreign protein disappeared from the circulation at just the rate that would be expected if no antibodies against it had been formed. At one time most of us believed that immunological paralysis could not be classified as an essential non-reactivity. Antibodies were probably formed, we believed, but were promptly bound by antigen present in vast excess. But the most recent work, notably from A. H. Coons's laboratory, makes this interpretation rather doubtful, for refined methods have so far failed to reveal that any immunological reaction is afoot. These observations have given rise to the hope that paralysis and tolerance of soluble antigens may be indistinguishable phenomena. The problem now to be decided is whether or not the inception of tolerance in the narrower sense depends on some quantitatively distinctive property of immature lymphoid cells. Are embryonic cells specially easy to paralyse, for example, or, what comes to the same thing, is it specially difficult to make adult cells tolerant? I know that work bearing on this problem is in progress in Coons's and Mitchison's laboratories. For many reasons—one of them the need to distinguish between the doses of antigen needed for the inception and the maintenance of the unresponsive state—the problem is by no means so easy to tackle as might appear at first sight. It is a matter of some importance that a quantitative study of the same kind should be made of tolerance of foreign tissue grafts. If I may refer once again to the experiment described at the beginning, we can be sure that an adult *A*-line mouse will not be made tolerant of *CBA* tissues by the injection into it of a proportionate multiple of the number of *CBA* cells that would have sufficed if their recipient had been newly born; but we still do not know whether a disproportionately large number of *CBA* cells might not confer tolerance on a mouse, say, ten days old. However, the possibility that tolerance and paralysis are no more than quantitatively distinguishable, if even that, makes it more urgent than ever before to prepare the antigens that excite transplantation immunity in an adequately potent form.

Two other forms of non-reactivity should be mentioned. One is the specific tolerance of tissue grafts which may be conferred upon a totally irradiated mouse the hæmatopoietic tissues of which have been restored by an injection of foreign bone-marrow cells. J. F. Loutit has suggested that the phenomenon is akin to tolerance in the narrower sense defined by our own experiments, but here, too, the analogy with immunological paralysis is not far to seek. Curiously enough, the encouragingly long survivals of kidney homografts reported by our surgical colleagues in Boston and Paris[17] have been brought about by the use of rather lower doses of whole-body irradiation than experience with mice might have tempted one to regard as essential. Perhaps the behaviour of inbred and homozygous mice is not the best theoretical guide to what may be expected of animals so obstinately heterozygous as human beings. Is it possible

that 'radiation induced tolerance' might be easier to secure when the mouse donors are hybrids of type X/Y and the recipients hybrids of type Y/Z? This model is also unrealistic, but more akin in principle to the genetic situation that human beings confront us with in real life.

Finally—I have put it last because it is the least easy to classify, though it might turn out to be the paradigm of all such phenomena—I must mention the inhibition of drug allergy described by M. W. Chase and M. Sulzberger[14]. Guinea pigs fed by mouth with, for example, pieryl chloride, no longer develop a cutaneous hypersensitivity of the delayed type on the application of that substance to the skin. Analysis has shown that this, too, is an essential non-reactivity. Many of us nourish the hope that a similar principle might be turned to good account in transplantation immunity, if it should prove possible to prepare a 'haptenized' derivative of the antigens that cause it to come about.

Biological Significance

Tolerance is a natural phenomenon, though its natural occurrence among chimeric twins may be something of an oddity. Has it any wider zoological significance?

The immunological defences of the body are directed against foreign matter. It is not at all common for an animal to react on the native ingredients of its own body. Burnet was the first to realize that this is not a state of affairs to be taken for granted, but something that calls for a special explanation; and it was his attempt to explain it that led him to predict that antigens which impinged upon an animal sufficiently early in its life should come to be accepted as if they were its own. Now that tolerance is an established fact we may turn his argument the other way about. Tolerance is ideally well qualified to provide a built-in natural safeguard against the danger that an animal might be sensitized or immunized by the constituents of its own body, and this may turn out to be its biological *raison d'être*[16]. If this argument is true, then the only substances capable of exciting auto-immune reactions should be those which never normally have access to centres of immunological response, so that the body has no opportunity to learn to tolerate them. I do not know of any evidence that contradicts this inference.

Tolerance makes one think anew about the special relationship that holds between a mammalian mother and its unborn young. There are hints in the literature that a mammalian infant may be specially tolerant of antigens of maternal origin, and evidence of such a relationship should be found more readily among human beings than elsewhere; for unlike rats and mice we have a long gestation period, and unlike sheep and cattle our foetal membranes are permeable by at least some molecules as large as proteins. Yet it seems most unlikely that maternally induced tolerance should be of regular or well-defined occurrence. The permeation of the foetus by foreign antigens gaining access through the mother might weaken its resistance in later life to infectious disease (we may recall here the significance read by Burnet and Fenner into Traub's observations on lymphocytic choriomeningitis[8]). This is only one among half a dozen reasons why traffic between maternal and foetal circulations should be under very close control. The occurrence of runt disease makes it, of course, unthinkable that the barrier between mother and foetus should be easily penetrable by anything so large as maternal cells.

Theories of Tolerance

Burnet and I have agreed on a division of labour which absolves me from speculating on the causes of the various kinds of essential non-reactivity I have described. Tolerance, like the secondary response and the nature of immunological 'memory', has become something of a testing ground for theories of the immune response. It must be said that the occurrence of tolerance does not yet follow from any hypothesis of the nature of the immune response that has been verified by *independent* means. Far too much is still uncertain. We do not yet know whether any one antibody-forming cell is potentially capable of making any antibody within the organism's immunological repertoire or whether the competence of any one such cell is restricted to a sub-class of the reactions that can be engaged in by the organism considered as a whole. We do not yet know whether the act of synthesis undertaken by an antibody-forming cell is strictly and specifically underwritten by the cell's genetic make-up or whether, in J. Lederberg's terminology, the instructions that govern that act of synthesis are imparted by the antigen itself. If it should be true that the antigen does no more than choose between one set of pre-existing instructions and another, we still do not know whether those instructions are already present in the zygote and therefore part of the legacy of its descendants, or whether they must be added to (by mutation, necessarily) during the course of growth. Finally, we do not even know whether the antitheses as I have put them are wisely so put or not. But it is the study of tolerance that has raised these questions in a specially urgent form[18], and which, in due course, will make an important contribution to their answers.

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NEWS and VIEWS

New Year Honours

THE following names of scientists and others associated with scientific and related work appear in the New Year Honours list :

Baron : Sir Alexander Fleck, chairman of the Advisory Council on Research and Development, Ministry of Power, and of the Nuclear Safety Advisory Committee, for public services.

C.H. : The Earl of Limerick, chairman of the Medical Research Council.

Knights : Dr. Christopher H. Andrewes, deputy director, National Institute for Medical Research ; Prof. Alfred C. B. Lovell, professor of radio astronomy, University of Manchester, and director of the Jodrell Bank Experimental Station ; Alexander Oppenheim, vice-chancellor of the University of Malaya ; John N. Ritchie, chief veterinary officer, Ministry of Agriculture, Fisheries and Food ; Dr. Alan H. Wilson, a deputy chairman and managing director of Courtaulds, Ltd. ; Prof. Brian W. Windeyer, professor of radiology, University of London, dean of Middlesex Hospital Medical School ; Dr. Alfred E. R. White, of Toorak, Victoria, Australia, for philanthropic services to the advancement of culture and the development of medical research.

C.B. : H. A. Sargeaunt, deputy chief scientist, War Office ; W. H. Stephens, director-general of ballistic missiles, Ministry of Aviation.

C.M.G. : W. F. Searle, chief statistician, Colonial Office ; Prof. S. Sunderland, professor of anatomy, University of Melbourne, chairman of the National Radiation Advisory Committee ; Prof. A. D. Trendall, master of University House and deputy vice-chancellor, Australian National University, Canberra.

C.B.E. : J. B. Alexander, director of the Geological Survey, Federation of Malaya ; G. Burdon, engineer surveyor-in-chief, Marine Division, Ministry of Transport ; J. Cook, director of agriculture, Sarawak ; Dr. E. H. Derrick, deputy director, Institute of Medical Research, State of Queensland ; G. C. I. Gardiner, technical director, De Havilland Aircraft Co., Ltd. ; Prof. R. B. Green, emeritus professor of anatomy, and lately dean of medicine, King's College, University of Durham ; W. A. Grinsted, director of the West Indies Meteorological Service ; Prof. C. H. Stuart-Harris, professor of medicine, University of Sheffield ; G. K. B. Hay, formerly director of agriculture, State of Western Australia ; Dr. G. A. C. Herklots, principal of the Imperial College of Tropical Agriculture, West Indies ; F. T. Ingham, lately director of Geological Surveys, Cyprus ; Dr. D. Dilwyn John, director of the National Museum of Wales, Cardiff ; R. H. Jones, chief electrical engineer, Crown Agents for Oversea Governments and Administrations ; C. E. T. Mann, formerly director, Rubber Research Institute of Malaya ; W. J. M. Menzies, member of the Advisory Committee on Fishery Research ; Prof. J. C. Mitcheson, professor of mining, University of London (Imperial College, Royal School of Mines) ; Prof. J. A. Manché, vice-chancellor and rector magnificus of the Royal University of Malta ; E. F. Newley, deputy director, Atomic Weapons Research Establishment, Aldermaston ; A. A. Rubbra, technical director, Rolls-Royce, Ltd. ; G. C. Turner, a principal actuary, Government Actuary's Department ; E. J. Vaughan, a deputy chief scientific officer, Admiralty ; G. E. Watts, principal, Brighton Technical College ; Prof. A. W. Williams, professor of medicine, Makerere College, Uganda ; H. Woods, H.M. deputy chief inspector of factories, Ministry of Labour.

Biochemistry at Trinity College, Dublin : Prof. B. Spencer

DR. BRIAN SPENCER has been appointed to the chair of biochemistry at the University of Dublin, established in place of the chair held for his life-time by the late Dr. W. R. Fearon (obituary, see *Nature*, **185**, 283 ; 1960). Dr. Spencer studied at the University of Liverpool and was awarded a B.Sc. with first-class honours in biochemistry in 1948, and a Ph.D. in 1950 following postgraduate work with Prof. R. T. Williams at Liverpool and St. Mary's Hospital Medical School. Later, he joined the staff of the Department of Physiology, University College of South Wales and Monmouthshire, Cardiff, and in 1956 transferred to a newly created Department of Biochemistry under Prof. John Pryde. In 1956–57, Dr. Spencer spent a year's leave of absence working on biochemical cytology with Dr. E. V. Cowdry at Washington University Medical School, St. Louis. Dr. Spencer developed an interest in sulphate esters during his postgraduate work in the field of detoxication, and at Cardiff he became well known for his work on sulphatases and on sulphate ester synthesis. In recent years he has extended his interests to the biochemistry of epithelia and teratogenesis.

Bacteriology at the London School of Hygiene and Tropical Medicine : Prof. E. T. C. Spooner

PROF. E. T. C. SPOONER recently gave up the chair of bacteriology at the London School of Hygiene and Tropical Medicine to become full-time dean of the School. He was educated at Epsom, St. Bartholomew's Hospital and Clare College, Cambridge, where he gained a Foundation Scholarship, and was elected a Fellow in 1929. Apart from two years as a Commonwealth Fellow at Harvard (1929–31), he spent the best part of twenty years at Cambridge as tutor, and as demonstrator and lecturer under H. R. Dean in the Department of Pathology. Many probably expected him to live and die a Cambridge don. In 1947, however, he was called to the chair at the London School of Hygiene and Tropical Medicine, which he has held until the present time. His contributions lie within the field of virus diseases, including dog distemper and mumps, and of tetanus and other anaerobe infections and of hospital cross-infection. During the Second World War he held a temporary commission and visited the Middle East to advise about hepatitis and other problems. His importance to medicine has particularly been that of the wise counsellor. He was a member of the Medical Research Council from 1953 until 1957 and has been a much valued member of a number of its committees. From 1949–55 he was editor of the *Journal of Hygiene*.

Prof. D. G. Evans, F.R.S.

DAVID GWYNNE EVANS has been appointed to succeed Prof. Spooner in the University chair. He is a science graduate of the University of Man-

chester. He began work on bacteriology in Manchester under Prof. H. B. Maitland in 1934, devoting particular attention to whooping cough. His best-known work is in the field of whooping cough —the antigens of *Haemophilus pertussis* and their relation to immunity. In 1940 he joined Percival Hartley in the Division of Biological Standards at the National Institute of Medical Research at Hampstead, where he worked on the standardization of toxins, especially those of gas gangrene. In 1947 he returned to Manchester to become a reader in Maitland's department. In 1955 he returned to the National Institute at Hampstead when it became urgently necessary to devise means for ensuring the safety and potency of poliomyelitis vaccines. This, coming at the time of the "Cutter incident", was a difficult task; we owe much to Evans and his colleagues for the fact that the British polio vaccines are second to none. In 1958 he succeeded Miles, taking charge of the Biological Standards Division. The value of his work was recognized a year ago when he was elected a Fellow of the Royal Society.

The New York Academy of Sciences: President

Dr. Frederick Y. Wiselogle, assistant director in charge of chemical research in the Squibb Institute for Medical Research, New Brunswick, has been elected president of the New York Academy of Sciences. During 1948 Dr. Wiselogle was awarded the Presidential Certificate of Merit for his work on anti-malarial drugs.

New Honorary Life-Members

The following were elected to honorary life-membership of the Academy: Sir Edward Dodds, Courtauld professor of biochemistry, University of London; Sir Alfred Lovell, professor of radio-astronomy, University of Manchester, and director of the Jodrell Bank Experimental Station; Dr. Giulo Natti, director of the Institute of Industrial Chemistry, Polytechnic Institute of Milan; Dr. Franz Buchner, director of the Pathological Institute, University of Freiburg; Dr. J. J. Trillat, director of research at the National Centre for Scientific Research, Paris. The total number of honorary life-members in the Academy is limited to 100. With the election of these five, the total number of honorary life-members of the New York Academy of Sciences is now 85.

Awards

Isidor B. Laskowitz, 284 Eastern Parkway, Brooklyn, has been awarded the D. B. Steinman Award of 500 dollars for his description of a new concept for a simple landing aircraft incorporating high speed, stability and vertical take-off without the use of rotors. Dr. Minoru Tsutsui, of the New York University College of Engineering Research Division, has been awarded the A. Cressy Morrison Award of 400 dollars for his description of the principles governing coupling of molecules through stoichiometric and catalytic activity.

European Co-operation in Space Research

In reply to a question in the House of Commons on December 12, the Parliamentary Secretary to the Ministry of Aviation, Mr. G. Rippon, said, on behalf of the Minister for Science, that recent negotiations in Geneva had led to the signature by ten countries, namely, Belgium, Denmark, France, Great Britain, Italy, the Netherlands, Norway, Sweden, Switzerland and Spain, of an agreement setting up a Preparatory Commission to study the possibility of establishing a European organization for co-operation in space research. The Geneva Conference expressed the hope that the Preparatory Commission would consider the closest possible co-operation between any organization which might later be formed for space research in Europe and any collaborative organization between European States for the development of a launcher. Mr. Rippon added that Britain would keep in close touch about the matter with the Commonwealth and particularly with Australia.

Student Grants in Great Britain

In a written answer in the House of Commons on December 19, the Secretary of State for Scotland, Mr. J. S. Maclay, said that the revised scale of parental contributions for university students announced by the Minister of Education on December 1 would come into force in Scotland in October 1961, and would apply to university students, students at colleges of education and students taking advanced courses in colleges of further education. It is the Government's intention to have the new rates of maintenance allowances in operation not later than October 1962, but an interim improvement of Scottish allowances will be made in October 1961. Mr. Maclay said he would consult the local authority associations about the complex problems involved in putting these arrangements into effect, and also about the small number of further education students taking shorter courses with lower entrance qualifications who would not be covered by these arrangements. The Government also proposes to accept the Anderson Committee's recommendations that no deductions should be made from grants from public funds in respect of an award holder's personal income, including income from scholarships and prizes, up to £100 a year, and that there should be no restriction on the student's freedom of choice of any university in Great Britain.

In replying for the Government in an adjournment debate on State scholarships in the House of Commons on December 21, the Parliamentary Secretary to the Ministry of Education, Mr. K. Thompson, pointed out that the acceptance of the Anderson Committee's recommendation, that a student who obtained a pass in a minimum of two subjects at Advanced Level in a General Certificate of Education examination and was accepted by a university for a place should qualify for an award, should make a separate system of awards to ameliorate financial hardship unnecessary. Under the new system, the financial basis of the State scholarship system is removed. Moreover, the State scholars are not by any means the only honours students in the universities, and he believes that the incentive to get a place in a university in an increasingly competitive field will itself provide a stimulus to students to give of their best in their sixth-form days. The Government is now ready for discussions with the responsible authorities of the universities and colleges to see how far the new arrangements could help to ameliorate the ill-effects of the pressures which such competition imposes on sixth-form curricula, and is seeking opinions on some proposals advanced by the Secondary Schools Examinations Council. Mr. Thompson said that under the new system, benefactors might be encouraged to offer prizes at more of the civic universities, and this might help to diminish the attraction of Oxford and Cambridge for the best

students. Further, while it is proposed that the technical State scholarships should disappear, the Government proposes to retain the mature State scholarships, mainly in their present form. He agreed with Mrs. Eirene White that there are real advantages in British students following courses at colleges in other parts of the Commonwealth, and said it is hoped before long to announce a successful outcome to discussions with local authorities on Commonwealth scholarships and the tenure of awards in Commonwealth universities.

Service to Teachers

From time to time there has appeared in the columns of *The Schoolmaster*, the journal of the National Union of Teachers, a feature article entitled "Treasure Chest for Teachers". The purpose of this feature has been to offer information about associations of an educational nature, various embassies, consulates, and industrial organizations which are willing to supply certain services and teaching material free or at reduced rates for the use of schools and training colleges. From the number of inquiries about this material received at the headquarters of the National Union of Teachers and the organizations concerned, it became apparent that teachers and school librarians, in primary and secondary schools as well as in training colleges, were finding the feature sufficiently useful for it to be re-issued in permanent form. The National Union of Teachers has now issued the material as a booklet to all engaged in education who may find it useful (Pp. 94. London: Schoolmasters Publishing Co. 1960. 3s.).

Endorsed Certificates in Biology

Results of examinations for endorsed certificates in biology are reported in the *Institute of Biology Journal* (7, No. 4; October 1960). In 1960, 106 candidates sat for examinations for the endorsed certificates at Ordinary Level. The examinations were taken in eleven colleges and 63 people were successful. The higher endorsed certificate papers were taken in seven colleges by 25 candidates, of whom 23 were awarded certificates. The technical colleges participating were Acton, Belfast, Bristol, Brunel, Cambridge, Ewell, Guildford, Heriot-Watt (Edinburgh), High Wycombe, Nottingham and Paisley (West of Scotland). Courses are now established at Stockport and Norwich City College.

Teaching Mathematics in the Junior School

Many primary school teachers and lecturers who teach mathematical methods in training colleges and university education departments will welcome a recent publication by the National Union of Teachers (Mathematics in the Junior School. By J. S. Flavell. Pp. 28. London: National Union of Teachers, 1960). With the primary aim of making work understandable and so enabling the child to think, the booklet examines in detail the following fundamentals of a course outlined by Flavell: understanding of basic mathematical ideas, particularly number, quantity, size, notation and positional value; understanding of the meaning and significance of the fundamental operations of mathematics—addition and subtraction, etc.; the significance of zero; translation: this includes the ability to record in suitable form numerical relationships, the ability to translate from figure to word and *vice versa*, simple mathematical facts, statements and complete sentences (equations); generalization in mathematics; background, cultural studies of the growth through history of number ideas and practices, and of evolution of units of all kinds.

Journal of the International Union of Pure and Applied Chemistry

For many years now, decisions and recommendations made by the International Union of Pure and Applied Chemistry, particularly those on nomenclature, have been disseminated in the journals of participant countries. While this procedure has been reasonably satisfactory, the need for a more suitable medium of publication of these and other less-widely appreciated commission reports has become increasingly felt. At Paris in 1957 a Publications Committee was appointed to investigate the situation, and in 1959, at Munich, the Council decided to bring all its publications together in its own *Journal* under the guidance of an editorial advisory board. Because of the inevitable heterogeneity of the subject-matter to appear between the covers of this one journal, an arrangement was made whereby separate papers could be made available in pamphlet or book form. This first issue is largely concerned with publication of the proceedings of the symposium on "Radioactivation Analysis" held in Vienna during 1959, but also contains notes on the organization and functions of the International Union of Pure and Applied Chemistry and several reports. These reports describe: recommended standards for the microdetermination of carbon and hydrogen; the calibration of wave-length and photometric scales for non-recording spectrophotometers; the standardization of *p*H and related terminology; terminology of scales of working in microanalysis; terminology for use in relation to precision balances; preliminary recommendations on nomenclature and presentation of data in gas chromatography. Further issues are to deal *inter alia* with: dissociation constants for organic acids in aqueous solution; proceedings of the symposium on "Thermodynamics" (Firtzens-Wattens, 1959); proceedings of the symposium on "Tolerated Limits of Toxic Substances in Industry" (Prague, 1959). While one cannot but deplore the ever-increasing spate of scientific journals, the decision of the International Union to produce its own official journal should receive wide approval. It should be of great value to all chemists, and this first issue reveals that the *Journal* will indeed attract serious attention. It is understood that the *Journal* will be published at irregular intervals but will comprise four issues per volume. The subscription-rate is £6 per volume. While no decision is announced, it would appear that the usual trilingual presentation in English, French or German is to be observed.

Bernice P. Bishop Museum, Hawaii

The annual reports of many museums have recently been entirely re-cast, and in many instances are highly attractive and form interesting reading. The report for 1959 of the Bernice P. Bishop Museum, Honolulu, Hawaii, is entitled "Prelude to a Plan" and is an excellent example of the 'new look' in such statements (Pp. 32. Honolulu, Hawaii: Bernice P. Bishop Museum, 1960). The year was a prelude to a five-year plan for the whole Museum and covered such diverse aspects as the construction of a planetarium observatory, the inauguration of the Pacific Science Information Centre, and a retirement and annuity

plan for the staff. The report shows clearly how the combined efforts of trustees, staff, volunteers and friends at home and abroad have carried the Museum through its seventieth year of service. The report is well illustrated with appropriate photographs of activities in the Museum.

The Water Research Association

THE period (1959–60) covered by the fifth annual report of the Water Research Association forms a milestone in the development of the organization for two reasons—it is the first year during which a grant has been received from the Department of Scientific and Industrial Research, and it is the last full year which the Association will spend in temporary accommodation at Redhill before moving to new laboratories at Medmenham (Pp. 24+4 plates. Redhill: The Water Research Association, 1960). A large part of the progress report of the Research Division, included with the Association's report, is concerned with laboratory experiments on factors affecting coagulation of suspended matter in water. At Medmenham, where a supply of water drawn from the Thames is available, it will be possible to carry out field trials on improved coagulation processes resulting from the laboratory work.

Problems of Ageing

BECAUSE little is known about the biological phenomenon of ageing and because of the problems which result from the increasing number of older people in the population, the U.S. National Institutes of Health have set up special programmes to stimulate and support research in all health-related aspects of ageing. As part of the research carried on within its own organization, the National Institutes of Health are conducting investigations into ageing in the Gerontology Branch of the National Heart Institute, located at the Baltimore City Hospitals in Baltimore, Maryland, and in the Section of Ageing of the National Institute of Mental Health, located in the Clinical Centre at Bethesda, Maryland. Within the research and training grant activity of the National Institutes of Health, there are many projects bearing directly on problems of ageing, ranging from investigations at the molecular level to investigations at the social level. Work on chronic disease in relation to the ageing process falls between these two extremes.

The Centre for Ageing Research, a component of the Division of General Medical Sciences, fosters additional investigations of all kinds of problems in ageing which are related to health. In addition to the research projects, both intra-mural and extra-mural, which are directly concerned with problems of the ageing process or ageing people, much of the research carried on or supported by the National Institutes of Health has an indirect or secondary bearing on problems of ageing. A booklet has now been prepared giving details of all the projects supported by the National Institutes of Health which have direct or indirect bearing on ageing (U.S. Dept. of Health, Education and Welfare: Public Health Service. Publication No. 761: Activities of the National Institutes of Health in the Field of Gerontology—Research Grant and Training Projects Active on January 31, 1960, and Intramural Research Projects carried on during calendar year 1959 (Washington, D.C.: Government Printing Office. Pp. v+41. 30 cents).

Current Medical Research

A VALUABLE document by the Medical Research Council contains reprints of the articles submitted by the Medical Research Council to Parliament for the year 1958–59 ("Current Medical Research". Pp. v + 56. (London: H.M. Stationery Office, 1960.) 3*s.* 6*d.* net). The subjects considered include the following: occupation and coronary heart disease; studies on the chemotherapy of tuberculosis in East Africa and India; clean air in operating theatres; human population genetics; chromosome abnormalities and disease in man; new applications of electron microscopy; the structure of viruses; the structure of muscle in relation to the mechanism of contraction; interferon: the prospects for an anti-viral agent in man; the arthropod-borne viruses; the plasma kinins and some factors in the problem of inattention.

Zoology of Persia

IT is, perhaps, surprising that the zoology of Persia is very imperfectly known: the country appears to have been neglected by Western zoological explorers, who have passed it by in concentrating on more distant lands to the east. A recent paper by Dr. Xavier Misonne describes the topography of Iran and the distribution of its mammalian fauna (Institut Royal des Sciences Naturelles de Belgique. Mémoires. Deuxième Série, Fasc. 59: Analyse Zoogéographique des Mammifères de l'Iran. Pp. 157+3 planches. Bruxelles: Institut Royal des Sciences Naturelles Belgique, 1960). Dr. Misonne was fortunate in being able to participate in the field investigations on the problem of plague transmission sponsored by the World Health Organization. These were particularly concerned with the distribution and biology of the rodents of the genus *Meriones*, to which the author gives special attention. As a result of several visits to the country, Dr. Misonne is able to give a comprehensive account of the distribution and ecology of the mammalian fauna, but he specifically disclaims that his work attempts a systematic revision of the Iranian species. His paper is illustrated with numerous distribution maps and several well-produced plates.

Tunnelling between Semiconductors

THE laboratories of both A. D. Little (Cambridge, Mass.) and the General Electric Company (Schenectady) have extended (*Phys. Rev. Letters*, **5**, 461, 464; 1960) the latter's recent work on tunnelling at low temperature through a very thin insulator between two metals (*Phys. Rev. Letters*, **5**, 147; 1960) down to temperatures at which both metals are superconducting. They prepared metal-insulator-metal sandwiches by evaporating a thin film of aluminium (transition temperature (T_c) of 1·2° K.) on to glass, exposing it to air to produce an oxide film about 20 Å. in thickness, and superimposing an evaporated layer of a second superconductor such as lead (transition temperature of 7·2° K.) or indium (transition temperature of 3·4° K.). The relationship between current (I) passed and voltage (V) applied across the sandwich then assumes particular interest below 1·2° K. at voltages around 1 mV., having a region for which dI/dV is negative—reminiscent of an Esaki (tunnel) diode for a voltage $\sim 0{\cdot}2$ V. Analysis of the relationship has enabled estimates to be made of the distribution of states of electrons in the super-

conductors, and of the small energy-gap which modern theory postulates as a characteristic of superconductors; values of the gap of $4 \cdot 3\ kT_c$ and $3 \cdot 6\ kT_c$ are quoted for lead and indium, respectively. The region of negative resistance disappears when either metal of the sandwich is taken above its transition temperature; an applied magnetic field, by its control of T_c, can therefore modify the I/V relationship, and at 1° K. the current passed by one sandwich for an applied voltage of 0·2 mV. could be changed by a factor of 10^5. These effects thus make possible active devices capable of amplifying, and of acting as bi-stable switches.

The Torald Sollmann Award in Pharmacology

Wyeth Laboratories of Philadelphia have established the Torald Sollmann Award in Pharmacology to commemorate the pioneer work in the United States of Dr. Torald Sollmann in the fields of pharmacological investigation and education. The Torald Sollmann Award consists of 2,500 dollars and a medal, and will be awarded for significant contemporary contribution to the advancement and extension of knowledge in the field of pharmacology. The Award is open to all scientists working in the field of pharmacology including, but not limited to, individuals from academic institutions, foundations, government and industrial and research organizations, regardless of age, sex or nationality. It will be given for originality and uniqueness of approach as well as development of the new concepts, theories and techniques which constitute a definite, mature and significant contribution to the extension and advancement of contemporary pharmacological knowledge. Not more than one Award will be made annually. Nominations for the Award must be submitted to the secretary of the Society (who is at present Prof. R. M. Featherstone, Department of Pharmacology, University of California, San Francisco 22) to be forwarded to the Chairman of the Torald Sollmann Award Committee not later than January 15 of each year to be eligible for consideration for an Award during the ensuing year. The first Award will be made at the 1961 autumn meeting of the Society in Rochester.

University News :

Birmingham

The following appointments have recently been made: G. R. Izaak, to be research associate in nuclear physics in the Department of Physics; Dr. C. F. Wells, to be lecturer in the Department of Chemistry; Dr. F. Bakhtar, to be lecturer in the Department of Mechanical Engineering; R. H. Hollier, to be Tube Investments Senior Research Fellow in the Department of Engineering Production; Mr. J. W. Fortey, to be lecturer in the Department of Civil Engineering; Mr. D. E. N. Davies, to be Associated Television Fellow in the Department of Electrical Engineering; Mr. B. Henderson, to be William Gibbins Research Fellow in the Department of Physical Metallurgy; Dr. A. I. Rees, to be Imperial Chemical Industries Fellow in Geophysics, in the Department of Geology; Dr. C. E. Rowe, to be Caroline Harrold Research Fellow in the Department of Physiology.

Edinburgh

The following have been appointed to lectureships: Dr. T. D. Patten (engineering) and Mr. D. C. Malcolm (forestry). Dr. J. L. Holmes and Dr. A. J. Charlson have been appointed Imperial Chemical Industries Research Fellows for three years.

London

Titles of professor in the University of London have been conferred on Dr. N. A. Barnicot (physical anthropology), in respect of his post at University College; Dr. L. F. Lamerton (biophysics as applied to medicine), in respect of his post at the Institute of Cancer Research: Royal Cancer Hospital. Titles of reader in the University of London have been conferred on Dr. R. H. Garstang (astronomy), in respect of his post at University College; Dr. M. K. Wells (geology), in respect of his post at University College. Dr. M. D. Milne, lecturer at the Postgraduate Medical School of London, has been appointed to the University chair of medicine tenable at Westminster Medical School.

The following appointments to readerships have been announced: Dr. F. A. Goldsworthy (applied mathematics), tenable at Queen Mary College as from January 1, 1961; Mr. E. J. Ambrose (physical chemistry), tenable at the Institute of Cancer Research: Royal Cancer Hospital; Dr. R. Creese (physiology), tenable at St. Mary's Hospital Medical School; Dr. L. Miles Jackman (organic chemistry), tenable at the Imperial College of Science and Technology; Mr. M. J. Way (applied entomology), tenable at the Imperial College of Science and Technology; Dr. G. M. Timmis (chemistry), in respect of the post held by him at the Institute of Cancer Research: Royal Cancer Hospital; Dr. C. R. Webb (mechanical engineering), in respect of the post held by him at Queen Mary College; Dr. H. I. Winner (bacteriology), in respect of the post held by him at Charing Cross Hospital Medical School.

Announcements

Sir Cyril Hinshelwood, Dr. Lee's professor of chemistry in the University of Oxford and past president of the Royal Society, has been awarded the Medal for 1961 of the Society of Chemical Industry. The Medal, a senior award of the Society, is presented every two years for conspicuous services to applied chemistry by research, discovery, invention or improvements.

Dr. William O. Baker, vice-president of research at the Bell Telephone Laboratories, has been elected to the Board of Trustees of the Rockefeller Institute. Dr. Baker is also chairman of the National Science Information Council.

The five hundred and seventy-seventh meeting of the American Mathematical Society will be held at Hunter College, New York, N.Y., on February 25. Further information can be obtained from Everett Pitcher, American Mathematical Society, 190 Hope Street, Providence 6, Rhode Island.

A symposium on "Temperature—its Measurement and Control in Science and Industry" is being jointly sponsored by the American Institute of Physics, the Instrument Society of America and the National Bureau of Standards. The symposium will be held at Columbus, Ohio, during March 27–31. Further information can be obtained from V. W. Sikora, Instrument Society of America, 313 Sixth Avenue, Pittsburgh 22, Pennsylvania.

THE FORM OF NEW UNIVERSITIES IN BRITAIN

THE second session of the Conference of Universities of the United Kingdom, held in London on December 10, discussed the problem of "New Universities".

In the first half of the present century the growth of the number of university students has been comparatively slow in Britain, and the creation of new university institutions has depended largely on local initiative and finance. The university colleges have had to depend mainly on students from their immediate region, and their academic staff have had to work to the curricula and examinations of their parent, the University of London.

In the past few years the situation has been radically transformed; the establishment of the University College of North Staffordshire, with frankly experimental ideas, set the tone, and considerations of national prestige, the popular demand arising from new prosperity, and the demands of industry and defence have all contributed to a change whereby new institutions can be established with almost 100 per cent State aid for buildings, equipment and salaries, and institutions which will be free to plan and control their own courses and which will be free to experiment as boldly as they wish. These institutions are receiving abounding goodwill and assistance, from the University Grants Committee, local authorities, industry, other cultural institutions, the general public and the staffs of existing universities through the Association of University Teachers.

The two main addresses of the conference had a contrasting form, that of Mr. J. S. Fulton, principal of the University College of Sussex, dealing with the solutions of the problems of siting, staffing, curricula and policy as they were being worked out in practice and planning, and that of Prof. L. C. Sykes, of the University of Leicester, who spoke of the underlying principles which should guide a new university.

Mr. Fulton presented three main topics for discussion, namely, siting, size and function. The first topic appeared to offer two solutions, apart from considerations of population distribution: either the new university should be placed in some town like York, where there are already many other cultural institutions, or in some area with few in the hope that it would become the focus of cultural growth. Size would depend on two considerations: a minimum number of teachers to cover essential subjects would be 300, with a staff–student ratio of 1 to 10; this would give a minimum student body of 3,000. The maximum number would depend on the extent to which teaching methods and residential provision would offset the social disadvantages of larger numbers. Mr. Fulton thought that new institutions should grow rapidly, and he hoped that Sussex would reach 3,000 in ten years.

Mr. Fulton said that the growth of the student population and the new careers open to graduates require a new approach to teaching; he asked if courses devoted primarily to the development of scholars are necessarily appropriate to the 'new student'. At Sussex they are planning courses on lines which owe something to the experience of North Staffordshire. The courses in science have yet to be planned in detail, but in arts they are proposing a combination of an introductory first-year course with an intensive study of a subject in, not a department, but a 'school'. At first there are to be schools of European studies, English studies and social studies, to be followed with a school of international studies. In science, they are considering following the Cambridge pattern, with two main subjects examined at the end of three years, with subjects like the history or philosophy of science, with a further year in one subject for specialists. He hoped to see the development of courses that would link the faculties, biology with psychology or sociology with applied science.

Finally, Mr. Fulton said that he considered teaching should be based on some kind of tutorial system, which creates a close personal relationship between the teacher and the student.

There was much agreement in principle in the second address, by Prof. Sykes; but he also raised matters which provided much of the framework for the discussion which followed.

Education as a preparation for life rather than primarily as a professional training should be the aim of a new university, and to achieve this the university should devote energy to preparing the student's mind to use his course before he left school. This should be done through parents and teachers, as well as by means of mass media.

The problems of teaching for the citizens of the 'Affluent Society', who need more to control technology than to develop it, would depend on the attitude of mind of teachers. Teaching must no longer take second place in the interest of the academic staff, and research must no longer be the main criterion of academic worth. Successful teaching would depend in part on the creation of a community of learning in which domestic, architectural and landscape planning would be important, and in part on the development of a close personal relationship between the student and the teacher through forms of tutorial teaching. In the discussion that followed, these points were taken up by the Archbishop of York, Dr. Ramsay, who saw the aim of new universities as being the promotion of new knowledge as the prerequisite of the training of the imagination and the creation of a wholeness of understanding.

The question of the priority of teaching over research was a matter about which the conference disagreed, and both Prof. W. F. K. Wynne-Jones, of Durham, and Prof. P. J. Hilton, of Birmingham, argued that successful teaching depends on research, and that the two are not necessarily competing but complementary.

Another topic raised by Prof. Sykes which was widely discussed was that of the full participation of all the academic staff in the governing of the institution. He stated that if policy affects all, all should participate in its creation and that full information is the basis of loyalty.

This point was taken up in discussion by Prof. J. M. Cameron, of Leeds, who spoke of the importance of popular sovereignty and the dangers of oligarchy. Mr. T. G. Miller, of North Staffordshire, and Mr. H. Maddick, of the Association of University Teachers, supported these arguments, and the former urged the ending of the distinction between 'professorial' and 'non-professorial' teachers.

The problem of the independence of the new institution was raised by Prof. Sykes, and he emphasized the need for local financial and other support. In this he was supported with evidence by Prof. A. K. Stout, of Sydney, and Prof. J. E. Corry, the vice-principal of Queen's University, Ontario, both of whom dealt with some of the problems of political control. A reassurance was offered on this matter by Viscount Mackintosh of Halifax, who described the wide range of support given to Norwich by the University Grants Committee, by the general public, and by industry, commerce and the arts in the counties of Norfolk and Suffolk.

In contrast to the ideas of Mr. Fulton and in support of the thesis of Prof. Sykes, Prof. W. A. C. Stewart, of the University College of North Staffordshire, suggested that slow growth might in fact be the prerequisite of the development of successful interdisciplinary courses, and he pointed out that his institution now has 800 students after ten years growth.

The sense of the conference was—it had no formal resolutions or conclusions—that education in the 'new universities' should be liberal rather than technical in the narrow sense, and should educate the whole man, or woman, for life rather than for a career.

IMPACT OF MAN ON THE VEGETATION OF THE HUMID TROPICS

AN enterprising and successful symposium, convened by the Unesco South East Asia Science Co-operation Office, was held at Goroka, New Guinea, during September. It was brought to fruition through the generous hospitality of the Administration of Papua and the Territory of New Guinea and the unremitting efforts of J. S. Womersley, chief of the Division of Botany, Department of Forests, Lae. Thirty delegates attended from Australia, India, Indonesia, Malaya, Philippines, Sarawak, Singapore, Thailand, Great Britain, the United States, the Territory of Papua and New Guinea, and the South Pacific Commission. There were also twelve observers from the Territory, among whom Mr. H. P. Seale, district commissioner of the Eastern Highlands, was elected president of the symposium. Delegates arrived at Port Moresby, and on September 14 they were taken by charter-plane across the high mountains to Goroka at an altitude of 5,000 ft. Any doubts about the suitability of the site were soon dispelled by the comfort of the Goroka Hotel and the warm welcome from the district commissioner. In these inspiring surroundings, old in their display of the effects of early man in the valleys and on the mountain-sides, befitting the topic of the symposium, and new in the post-war growth of the administrative centre, a vigorous speech from the assistant administrator, Dr. J. T. Gunther, on behalf of the administrator, Brigadier D. M. Cleland, inaugurated the symposium. It was time, he said, to end not only the wars of man on man, but of man on beasts, and of man on vegetation. He struck a theme which forced itself into the chief recommendation of the meeting. The grandeur of Nature, the poverty of man, and the ideal of human rights surged into the panorama, for the object of the symposium was to bring together agriculturists, botanists, foresters, administrators, anthropologists and geographers in South East Asia and tropical Oceania.

Thirty-six papers had been presented and duplicated for previous study, and an efficient secretariat, brought from Port Moresby, reported the discussions in full. First, the physical and human backgrounds of the humid tropics were considered. Illness prevented Prof. W. A. R. Wikramateleke (Singapore) from giving the opening discourse, and in his place the aspects of climatology were presented by Prof. J. M. Blaut (Yale University), of soils and substrata by Dr. F. R. Fosberg (National Research Council, Washington), and of vegetation by myself. Prof. W. R. Geddes (University of Sydney) followed with a sympathetic approach to the human background, based particularly on his researches in Indo-China and Sarawak; he emphasized the 'c' in Unesco as the all-important socio-cultural element of human community and, indeed, the mark of man. The second topic, on the selection and cultivation of foods by early man, was introduced by Dr. J. Barrau (South Pacific Commission). He explained how early man was a practical geneticist selecting by taboo which prevented misappropriation and loss of valuable plants, thereby preserving the better yielders in the multitude of wild variety; the procedure was in striking contrast with the tendency to exterminate the valuable beasts. He was directing his studies to the problem of the bread-fruit tree, so widely cultivated in great variety, yet so obviously wild in New Guinea and the Melanesian islands. This important plant, too massive for interpretation in the herbarium, had to be studied in the arboretum, on which task he was bent. The problem of the sweet potato, chased by the peoples of New Guinea from valley to valley in almost maniacal destruction of the forest, raised considerable doubt on its supposed American origin. Fosberg presented his ideas on the origin of the coco-nut as a cultigen, the ancestral form of which botanists had not yet adequately contemplated. Mr. G. P. Keleny (Port Moresby) gave a detailed account of the basic food-crops of New Guinea. Dr. M. J. Meggitt (University of Sydney) explained his work on the native agricultural methods of the Western Highlands, showing the readiness with which new food-crops may be taken up. Mr. W. L. Conroy (Department of Agriculture, New Guinea), in comparing the effects of indigenous agriculture on soil-erosion and soil-deterioration with those of land-slides in forested country, considered that the damage supposed to be caused by deforestation might well be

exaggerated. He instanced the value of *Casuarina* in re-afforestation and soil-renewal in the Highlands. Dr. E. Quisumbing (Manila) related how the War had caused many new food-plants to be taken up in the Philippines.

Thirdly came the prolonged discussion on the effects of fire. To most delegates the Highlands presented endless deforestation followed by grassland and incessant burning. They were grateful to Mr. C. F. W. Julius (Port Moresby) for his careful analysis of native land-rights and usage in explanation of this scenery. Achieved in the first place by finger-nails, sticks and stones, and now accelerated by trenching tools, knives and matchets, with a wanton love of burning for fun, yet there was little evidence in New Guinea of deterioration into desert conditions. Nevertheless, the question was raised whether the replacement of forest by grassland caused a lower rainfall, such as certainly followed the wake of the gold-dredging in the Bulolo district. The discussion revealed the abundance of observation, the thicket of conjecture, and the lack of scientific inquiry.

Fourthly, in an able discourse on grasslands, Dr. W. Bryan (Brisbane) opened the session on the effects of grazing by the domestic animals of early man. New Guinea was a great contrast to Africa. Deforestation led to grasslands, but the absence of any indigenous grazing animals was reflected even in the reluctance among natives to adopt cattle-farming. Though all became grass under native agriculture, there was so little flesh. Anthropologists joined with agriculturists in presenting this problem of induced pastoralism, extending into tropical Oceania, as a concern for Unesco. A remarkable paper on the status of the pig in New Guinea was read by Julius on behalf of Mr. T. Aitcheson (Port Moresby).

Fifthly, the effects of shifting cultivation on the vegetation of the humid tropics were considered. Mr. J. A. R. Anderson (Sarawak) described the carefully planned experiment on regeneration of cleared areas which was in progress in Sarawak. Contributions were made by Dr. I. Y. Carey (Malaya) on the methods of the Temiar people, by T. Smitinand (Thailand), E. Quisumbing (Philippines), Y. Satyanaryan (India) and D. J. Kingston (Port Moresby). What had been an economical cycle for soil-regeneration seemed now in all countries to be becoming uneconomical as increasing population shortened the fallow-period through the demand for more land in use. It was much regretted that no observer from the Food and Agriculture Organization had been able to attend this meeting.

Sixthly, there was a discussion on the nature of secondary plant-communities arising from the activity of early man. Fosberg introduced the subject with a general review of such communities. Dr. R. G. Robbins (Canberra) outlined the results of his researches on the New Guinea grasslands; the full publication of this work will be most instructive. Mr. J. J. Havel (Rabaul) gave two valuable papers on his experimental approach to forest regeneration in eastern New Guinea. Mr. E. C. G. Gray described the remarkably efficient sylviculture of mangrove-forest developed on their own by the natives in the Gulf of Papua.

Lastly, the social and economic aspects of early man's action on the forests were considered. Mrs. K. V. Bailey described the dire effects of over-population in the denuded limestone country of Java. Keleny described the land-use patterns in Java. Dr. I. Polunin (Singapore) discussed the aspects of human health and disease under conditions of shifting cultivation which tend to prevent intensification of parasitic attack.

This symposium touched on many vast problems, requiring the attention of both pure and applied science. The delegates were, indeed, grateful to Mr. L. Mattsson, director of the Unesco South East Asia Science Co-operation Office, for his help in enabling them to escape from their isolation in this huge region, to join in such fertile discussion, and to formulate in a set of resolutions to Unesco what they considered to be the most urgent matters for investigation. Herein they were assisted in no small measure by the hospitality of the Administration which had arranged two magnificent excursions by air and land-rover to enable them to see the natural vegetation, the grand mountain scenery, the happy native peoples and, indeed, the fine work of the Administration itself in the Highlands of the Territory. We flew in the early morning around Mt. Wilhelm (15,400 ft.) and its alpine slopes, glacial valleys, and many peaks in a cloudless sky. We picnicked in *Nothofagus* forests. We were the guests of the beautiful township of Kundiava in the Upper Chimbu. We visited the property of the Halstrom Fauna Trust at Nondugl, where birds-of-paradise are bred—and what an ornithological field-station it would make. Mr. Womersley took the botanists to Kainantu, whence they visited the agricultural station at Aiyura on the way to the scenic junction of the Ramu and Markham valleys, and they were taken along the great Markham valley in a spectacular flight to their destination at Lae. Dr. Meggitt took the anthropologists and geographers to the northern district of Madang. Some of us stayed on in the busy verdant town of Lae on the shore of the Huon Gulf and enjoyed the beautiful Botanic Garden, which is under the direction of Mr. Womersley. It was a delight to find this seat of learning. Started on August 1, 1949, from a waste of wild sugar-cane, it now covers some 120 acres of lawns, flower-beds, plant-houses, woodland, and wooded streams. The new office and herbarium, which are planned, will be the Mecca of Melanesian botany, and the next ten years should see the perfection of the first. Here, several of us, from different lands, walked and talked, consolidating our views on the symposium; as Fosberg sagely remarked, a requisite of a delegate to such a pioneering conference should be his ability to stay a while and contribute to the knowledge of the country.

The eight resolutions concerning South East Asia and Tropical Oceania directed to Unesco dealt with the needs for: (1) the study of secondary plant-communities produced by human disturbance of the tropical forest; (2) the promotion of ethnobotany; (3) the effects of alien civilization on primitive peoples; (4) the study of the vegetation of limestone formations, so susceptible to destruction by fire and other causes; (5) the urgent need for programmes of consideration of natural resources; (6) the study of root physiology in the furtherance of soil science; (7) research into the socio-economic adaptation of recently contacted native people; (8) the convening of another symposium within the region of the South East Asia Science Co-operation Office in view of the stimulus given already to scientific and cultural understanding by the previous ones.

E. J. H. Corner

GAS CHROMATOGRAPHY

THE third international symposium on "Gas Chromatography" to be organized by the Gas Chromatography Discussion Group, this time in conjunction with the Society for Analytical Chemistry, was held at Edinburgh during June 8–10. More than 560 delegates attended the meeting, of whom more than 160 were from overseas. Three excellent receptions provided by the Organizing Committee, the Lord Provost of Edinburgh and the British Petroleum Co. were held in the evenings. Other items that added interest to the meeting were an instrument exhibition showing recent developments in commercial gas-chromatographic equipment, and visits to local industries arranged for the Saturday following the symposium.

The symposium was divided into three sections, Apparatus and Technique, Theory and Application, and General Applications, each being introduced by a well-known authority in the field. Preprints of the twenty-nine papers read were issued to delegates before the meeting, so authors had to point out only the highlights in their papers, thus giving more time for discussion. The full proceedings, edited by R. P. W. Scott, will be published by Butterworths Scientific Publications later.

The symposium began with a welcoming address by Prof. E. L. Hirst, of the University of Edinburgh, who described the impact chromatography had made on research in recent years. Dr. A. T. James, chairman of the Gas Chromatography Discussion Group, gave the opening address, outlining some of the more significant lines of research being currently followed. A report on the recent activities of the East German Working Group was read by Mr. H. P. Angele.

In the introductory lecture to the first session, "Applications and Technique", R. P. W. Scott pointed out areas where there was still much controversy among gas chromatographers. He emphasized the need for further work on column design, detectors and recording methods to improve both the speed and accuracy of quantitative analysis.

The recent very sensitive hydrogen flame and argon ionization detectors were the subject of the first session. L. Onkiehong and D. H. Desty reported investigations carried out on the flame ionization detector to determine the optimum design and operating conditions. Both concluded that the construction of the detector was not too critical except where the highest sensitivity is required. Similar results were found by R. C. Condon, who in addition compared the two ionization detectors. J. E. Lovelock investigated the design and operating parameters of the family of argon detectors. The triode detector, the most recently introduced, has a sensitivity of 10^{-14} gm./sec., about a hundred times better than that reported for the flame ionization detector. The sensitivity of all the argon detectors was found to be considerably reduced by the presence of trace amounts of hydrogen, nitrogen, oxygen, carbon dioxide and water in the argon. A comparison of integral and differential ionization detectors was made by S. Matousek.

Most of the discussion following the papers centred around the flame ionization detector. Many workers gave details of their own particular design, and it appeared that thick-walled jets which remained cool were preferable to those that glowed at red heat. F. van der Craats described how the linearity of the detector could be improved by using a cage rather than a disk as the upper electrode, and D. H. Desty stated that a small increase in sensitivity could be obtained by the addition of argon, nitrogen or oxygen to the hydrogen supply.

A disadvantage of the hydrogen flame-ionization over the argon detector is that an expensive impedance converter must be used to measure the low ionization currents produced. L. Onkiehong suggested that it may be possible to overcome this by the use of an a.c. polarizing potential ($\sim$ 100 c.p.s.) applied between the jet and a third electrode situated between the jet and collector. By this means a pulsed d.c. signal would be obtained at the collector which could be amplified by conventional methods. J. F. Smith gave details of an inexpensive amplifier using a cathode follower that was adequate where the highest sensitivity was not required.

An important feature not given sufficient attention by the majority of workers investigating detector performance was the determination of response factors for compounds of different type, to see whether any correlation exists between response and molecular structure. Difficulties in obtaining low known concentrations of vapours may be partly responsible for this, and the method for obtaining accurate concentrations down to 10^{-8} molar described by D. H. Desty should enable fuller work to be carried out in the future. Although no simple correlations were found in the papers read, in the discussion R. C. Condon pointed out that for the series of halogen compounds mono-, di- and tri-chloromethane the response of the flame ionization detector was proportional to the amount of hydrogen in the molecule, and F. Schild had found that the weight response for a number of oxygenated compounds was proportional to the product of the peak area and molecular weight. Both H. M. McNair and F. van der Craats compared the response factors that they had determined for hydrocarbons with those obtained by D. H. Desty and L. Onkiehong. A wide variation in relative response factors was apparent, and it may well be that these factors depend very much on the design and conditions under which the detector is operated.

The question of detectors of low concentrations of permanent gases arose, and T. B. Kent described how by using argon containing a few p.p.m. of acetylene as carrier gas concentrations of permanent gases in the p.p.m. region could be detected by the decrease in background signal produced. The use of the gas-discharge tube for the determination of small concentrations of impurity gases in argon was the subject of a paper read by B. Riley, and several industrial applications for an instrument of this type were outlined.

Following the discussion on detectors, attention turned to other developments in apparatus and technique. J. Boeke described the use of a modified form of frontal analysis in which the sample is continuously

introduced into the column considerably diluted in an inert carrier gas, and gave details of a detector arrangement that enabled curves approaching differential rather than the usual integral records to be obtained. I. Halasz described an integrator based on a new principle having a count-rate of 1·8 million pulses per minute for a full-scale recorder deflexion and which may be adjusted to correct automatically for the calibration factor of the substance detected. A comparatively inexpensive high-speed recording system, using a long-persistence cathode-ray oscilloscope, was described by R. P. W. Scott, and its value for recording fast separations illustrated by several traces showing separations carried out in less than 1 min.

The next section, "Theory and Application", was introduced by M. J. E. Golay, who discussed the relative importance of resistance to mass transfer in the liquid and gas phases with packed and capillary columns. He described how it should be possible to obtain lower height equivalent to a theoretical plate values by increasing the surface area of capillary columns without increasing the distance across which the solute molecules have to diffuse. This could be achieved by covering the inner wall of a capillary column with a finely divided clay before coating, and the improvement was demonstrated by showing a peak obtained for benzene before and after treating a column in this manner.

Capillary columns were the subject of the first two papers in this section, and investigations of the important operating and design features for achieving high efficiencies and high speed of analysis were reported by R. P. W. Scott and A. Goldup. Both discussed the effect of column diameter, film thickness and carrier gas on the height equivalent to a theoretical plate linear gas velocity curve and compared experimental results with those predicted by the Golay theory. R. P. W. Scott was able, by using carrier gases of different diffusivities, to show experimentally that, in accord with theory, the contribution from resistance to mass transfer in the gas phase to the total height equivalent to a theoretical plate was greater than that due to mass transfer in the liquid phase for solutes that are well retained. In general, a fair agreement between theory and experiment was found at gas velocities corresponding to the minimum height-equivalent to a theoretical plate, but at higher velocities the agreement was less satisfactory. M. A. Khan suggested that this may be due to the absence in the Golay equation of a term accounting for interfacial resistance between the gas and liquid phases, and reported that he had recently published a note[1] discussing this effect.

Examples of the efficiency and speeds of analysis achieved on capillary columns were reported by A. Goldup. Using a 600-ft. glass column, an efficiency of 300,000 plates had been obtained for a well-retained solute, and the separation of sixteen out of a blend of seventeen octane isomers was given as an illustration of the resolution attainable. The potentialities of capillary columns for high-speed analysis were demonstrated by chromatograms obtained using a recording system having a time constant of only a few milliseconds, which showed the separation of a blend of nine heptane isomers in 58 sec. and a simple four-component blend in 1 sec. C. P. Quinn presented equations derived theoretically defining the best conditions to achieve the minimum time of analysis and supported these with experimental data. The basic premise of using linear gas velocities higher than the optimum was criticized by J. H. Knox.

In the first of the two remaining papers of the morning session S. J. Hawkes discussed factors which limit the maximum operating temperature of stationary phases. Valuable data on several stationary phases were given, and in addition the use of substituted borazoles at high temperatures was suggested.

Structural analysis of hydrocarbons by capillary gas chromatography in connexion with the methylene insertion reaction was the subject of a paper presented by M. C. Simmons. The author described how by simply treating paraffin hydrocarbons with diazomethane under ultra-violet irradiation a mixture of homologues of one higher carbon number could be obtained, and illustrated the value of this for obtaining retention volume data on inaccessible hydrocarbons. For example, retention volume results had been obtained for nineteen branched nonanes from six readily available octanes. One particularly interesting separation reported by the author was that of the diasterioisomers of 2,3,4-trimethylhexane. In the discussion that followed, J. F. Smith described the separation of an alcohol and a sulphide into *meso*- and *dl*-forms by gas chromatography.

Progress on large-scale preparative columns was also reported at the symposium. F. H. Huytens described how the loss in efficiency observed with preparative columns of large diameter could be attributed mainly to column packing. By carefully filling columns so that radial diffusion is large and axial diffusion small, height equivalent to a theoretical plate value of 2 mm. could be obtained with 3-in. diameter columns capable of handling samples up to 1 gm. The use of preparative scale chromatography for examining complex organic materials was reported by T. Johns.

Details of an apparatus for obtaining accurate retention volume data were given in a paper presented by E. R. Adlard. Specific retention volumes for *cyclo*hexane and benzene on dinonylphthalate at temperatures from 48° to 110° C. were used to determine excess partial molar thermodynamic functions. For both systems investigated the excess partial molar entropies were found to be the predominant cause of the departure from ideality. In an interesting contribution to the discussion, J. C. Winters described some results obtained by R. L. Martin in which marked changes in the specific retention volume for hydrocarbons on polar stationary phases had been observed. To account for this, R. L. Martin had suggested that adsorption of the solute on the surface of the stationary phase contributes to the retention of the solute as well as solution in the stationary phase, and had shown that the former becomes of increasing importance as the percentage of stationary phase decreases.

The final papers presented in the section "Theory and Application" were by C. G. S. Phillips and his co-workers. They described the use of transition metal complexes and saturated solutions containing free undissolved tri-*o*-thymotide as stationary phases. The latter compound is of particular interest since it forms inclusion compounds with molecules of restricted width. By comparing retention data obtained for tri-*o*-thymotide with that for di-*o*-thymotide which does not form such complexes it was shown that the former selectively retards straight-chain compounds. The application of complexes of this type to give a separation according to molecular shape appears to be a most promising extension of gas chromatography.

The final day, devoted to "General Applications" of gas chromatography, was introduced by A. I. M. Keulemans, who described some of the results, using chromothermography, obtained by Prof. A. A. Zhoukhovitsky in the U.S.S.R.. By passing a ring furnace along the column during elution of the components it is possible to obtain symmetrical peaks using gas–solid chromatography at high sample concentrations. The technique enables samples of wide boiling-range to be examined, and has the added advantage that the temperature gradient and speed of the furnace offer additional parameters for controlling the separation.

The morning session was concerned mainly with the gas chromatography of inorganic compounds. Following a paper by G. Freiser describing the separation of the volatile chlorides of tin, titanium, niobium and tantalum at 200° C. on a 'Chromosorb' column coated with squalane, A. I. M. Keulemans mentioned that he had also separated volatile metal chlorides on an aluminium chloride-coated carbon column at temperatures up to 350° C. Both W. W. Brandt and J. Janak reported separating metals in the form of their acetylacetonates.

The chromatography of corrosive inorganic halogen compounds was the subject of two papers. T. R. Phillips employed a polytetrafluoroethylene capillary column coated with 'Kel-F' oils to separate mixtures of hydrogen fluoride, chlorine and chlorine trifluoride. A hydrogen-flame ionization detector, in which a platinum ring was maintained at red heat in the lower edge of the flame, was found suitable for detecting such inorganic compounds. Details of an apparatus incorporating a katherometer and automatic sampling valve, developed over a number of years for the analysis of plant streams containing highly reactive inorganic halide vapours, were given in a paper by G. Iveson.

Many other new and interesting applications of gas chromatography were described. J. Tranchant gave some results on the use of gas–solid chromatography for the qualitative and quantitative analysis of mixtures containing nitrogen oxides, and D. W. Hill described the application of gas chromatography to anæsthetic research. An illustration of how detailed information on gasolines may be obtained by a combination of liquid–solid and gas–liquid chromatography was illustrated by a number of chromatograms in a paper presented by S. T. Griffiths. C. G. Scott gave details of a method for investigating the stability of white oils. The oxidation products of low molecular weight are eluted with a stream of nitrogen, condensed in special traps and examined chromatographically.

In a discussion in which retention volume data were mentioned, J. F. Smith outlined a useful practical method for expressing all retention volume data relative to one standard 'theoretical' nonane.

In connexion with work on compounds of high molecular weight, J. Janak described how the composition of non-volatile materials could be investigated by the gas-chromatographic analysis of their pyrolitic products. The use of esters as high-temperature polar stationary phases for examining products encountered in polymer production was discussed by R. E. Roland-Jones, and two materials, polyethylene glycol adipate and ethylene glycol distearate, were found suitable for use at 250° C. C. G. Scott stated that he had been able to elute hydrocarbons containing up to fifty carbon atoms using alumina modified by treatment with alkali metal hydroxides as the column packing.

In the final paper of the meeting, G. R. Boreham described an apparatus suitable for fuel-gas analysis, which had as a special feature a multicell thermal conductivity cell that enables four columns to be operated in series with a detector at the outlet of each.

The meeting ended with an excellent summing up of the symposium by C. S. G. Phillips and a closing address by R. C. Chirnside, president of the Society for Analytical Chemistry.

A. GOLDUP

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ION EXCHANGE

ON December 2, the Permutit Co., Ltd., demonstrated a new film entitled "An Introduction to Ion Exchange". The programme was introduced by Mr. Walters, who gave a brief outline of the development and uses of ion exchange procedures, mentioning in particular the preparation of acid-resistant anion exchange resins. The film, which is in colour, commences by illustrating some of the uses of ion-exchange resins, including the production of potable water from sea water. On the molecular scale, the structure of polystyrene-based cation and anion exchangers is demonstrated using conventional atomic models, with the exchange process simply illustrated. On the macroscopic scale, the hydrophilic nature of dehydrated resin beads is shown by wetting them, followed by observation of the resultant swelling.

The three main operations of ion-exchange are then examined: (*a*) *Separation*. Here two coloured organic ions in solution are allowed to flow through a resin column. While the blue concentrates in a narrow band near the top of the column, the red is less strongly held, forming a wider band which could be eluted. (*b*) *Substitution*. The effect of passing a solution of potassium permanganate through a resin column in the chromate form is shown by a change in the colour of the solution from purple to yellow. (*c*) *Removal*. In this case a solution of a salt with two coloured ions, copper dichromate, is allowed to flow through a mixed-bed exchanger, resulting in the production of colourless 'de-ionized' water.

The exchange process is followed in more detail by a combination of demonstrations using copper dichromate and animated diagrams of sections through a resin bead in a flowing solution. A final survey of industrial aspects of water treatment completes the film.

Colour cinematography is an ideal medium for showing ion-exchange experiments, and in this sense the film is entirely successful. Nevertheless, although an attempt is made to discuss the mechanism of ion-exchange, a more critical and scientific approach would have been desirable. In particular, specific examples, in which the equilibria involved were considered in terms of quantitative data, would

have been valuable. Perhaps the most elegant use of ion-exchange is in the separation of the lanthanide and actinide elements. This aspect is almost completely ignored. Again, although emphasis is laid on the low conductivity of 'de-ionized' water, particularly by comparison with distilled water, an indication that the conductivity of laboratory distilled water is due almost entirely to dissolved carbon dioxide and ammonia would not have been out of place. Further, the 'de-ionized' water contains significant quantities of organic impurities, some of them surface-active and not detected by conductivity measurements. The film will certainly appeal to many potential users of ion exchange; whether it will appeal to students and research workers remains to be seen. "An Introduction to Ion Exchange" is a 16-mm. film with an optical sound track, and runs for 27 min. It is available on free loan to learned societies, colleges and schools, industrial associations, etc.: applications should be sent to the Permutit Co., Ltd., Permutit House, Gunnersbury Avenue, London, W.4.

SERVICE WITH OVERSEAS GOVERNMENTS

NEW arrangements for service with overseas governments are detailed in a White Paper issued by the Secretary of State for the Colonies*. For reasons indicated in an appendix, the British Government has rejected as impracticable the idea of an Overseas Service based on the United Kingdom. Such a Service would not solve the problem of the future prospects of members of the Overseas Civil Service, but the Government is examining the feasibility of establishing a Commonwealth Advisory and Technical Service as suggested by the Select Committee on Estimates. Under the new arrangements the Government will assume full responsibility for the cost of the inducement element, which is a necessary part of the emoluments of most expatriate officers, and a fresh review of the emoluments of the officers concerned will be necessary in many territories. For purposes of United Kingdom taxation, the additional pension payable to an expatriate officer, which stems from the inducement allowance, will be treated in the same way as existing pension, and the cost of that part of the pension will be borne by the Government. The Government will pay education and children's allowances similar to those payable to members of the Home Civil Service posted overseas, and will also meet half the passage costs required to enable children being educated outside the territory in which an officer is serving to visit their parents, or to be visited by their mother, once a year. The Government has also contributed to some compensation schemes now in force for loss of career on premature retirement, or taken account of their cost in considering what further financial assistance should be given, and for future schemes will share the cost equally with overseas Governments.

The scheme will come into effect in most territories on April 1, 1961, and will cover up to 21,000 pensionable and contract officers overseas at a cost to the British Government of £12–£16 million a year. Besides all existing Colonies and dependencies, it will be offered to Nigeria, Sierra Leone and Singapore, and to Northern Rhodesia and Nyasaland, but not to the Bahamas, Bermuda, Brunei and Hong Kong, where, for several reasons, this form of help is not regarded as appropriate, at least for the time being. The arrangements have been developed after consultation with overseas governments and staff associations and they are complementary to plans being vigorously pursued for staffing the public services by local officers in the territories concerned. The White Paper also emphasizes the value of overseas officers in technical assistance schemes, and a high-level technical assistance working party has been set up under Foreign Office chairmanship as a means of exchanging information and experience between departments and organizations engaged in technical assistance work. A sub-committee of this body will co-ordinate the recruitment activities of the Government for technical assistance posts, and the fullest consideration will be given to retiring and retired members of the Overseas Civil Service for all suitable vacancies. It is also proposed to give greater publicity to the Overseas Services Resettlement Bureau, which has already placed more than 1,000 of the 1,710 officers registered with it from July 1957 to mid-October 1960; it is pointed out that the Bureau could prove a very valuable source of man-power to industry and commerce, particularly to export industries seeking men and women with long and detailed knowledge of overseas territories.

As regards the future, the proportion of candidates appointed on contract terms through the Colonial Office has increased markedly in recent years and such appointments now constitute the great majority. Wherever possible the British Government plans to obtain recruits on loan from government departments, public corporations and local authorities, so that individuals can be certain of resuming their previous employment on returning to the United Kingdom. It is also hoped that individual service overseas will be accepted as an asset both to the employer and employee, and that employers will co-operate in facilitating the release of those able and willing to serve overseas and in re-absorbing them on their return.

Further to the above, the Colonial Office has now issued the report of the Public Services Conference held in London during March 1–10, 1960, to exchange information on measures taken or projected to build up local civil services in the African territories, which was initially a confidential document for consideration by the governments represented at the conference*. All, however, have since agreed that it should be published, and it has now been issued by the Colonial Office.

The agenda covered the general pooling of experience and a comparison of the measures adopted; a review of the facilities for secondary and university

* Colonial Office. Service with Overseas Governments. Pp. 22. (Cmnd. 1193.) (London: H.M. Stationery Office, 1960.) 1s. 3d. net.

* Colonial Office. Report of the Public Services Conference held in the Colonial Office, London, 1st to 10th March, 1960. Pp. iii+25. (Colonial No. 347.) (London: H.M. Stationery Office, 1960.) 3s. 6d. net.

education, including a comparison of scholarships schemes, training programmes; the exchange of information; the impact of localization on serving overseas officers; and the staffing problems which arise from the development of ministerial systems. The report makes no specific recommendations for governments to adopt, but indicates the important problems and the lines on which they might be tackled, leaving it for each government to reach its own decision after examining the report in the light of its own local conditions.

The report suggests that each government should make a general review of the whole range of problems arising from the need to staff the local civil service increasingly with local people and that standing arrangements should be made to keep under consideration the policy as it develops. Discussing the provision of sufficient numbers of educated men and women, the need to provide secondary and higher education before satisfying all the needs of primary education was emphasized at the conference, and it was urged that the balance of secondary and higher educational systems should be planned on the basis of regular authoritative surveys of the estimated needs for educated man-power undertaken by really first-class experienced persons. As regards courses of training in the United Kingdom, which in 1959 provided for some 2,300 places, more than half of which were taken by local Civil Service officers, the Colonial Office stated that it was very ready to consider the provision of new courses or *ad hoc* training attachments to meet the requirements of overseas governments. In regard to the training of technicians and especially the training of supervisors in technical work, the conference agreed that no good answer had yet been found to the problem of training supervisors rapidly, and that there was no real substitute for experience on the job. The Colonial Office agreed to undertake the preparation of periodical reports directing attention to any new developments of interest or importance, including lists of subjects for which courses were run by overseas governments, the first such report to be prepared in about 18 months. In discussing the special staffing problems which arise from the development of the ministerial system and, in particular, its bearing on the tripartite relation between minister, permanent secretary and heads of departments, stress was laid on the importance of enabling professional officers to contribute fully in the formulation of policy and of respecting their professional integrity. It was also agreed that the professional branch of the Service should have the primary say in assessing the qualifications of the professional staff and their deployment. It also recognized that it was essential to build up proper administrative backing for the professional work, and in particular to ensure good staff relations with professional officers in the field when establishment work was undertaken by administrative and executive officers at headquarters.

FIELD-ALIGNED IONOSPHERIC IRREGULARITIES AND THE SCINTILLATION OF SATELLITE RADIO TRANSMISSIONS

By D. G. SINGLETON, G. J. E. LYNCH and Dr. J. A. THOMAS

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MANY investigations have been made of the nature of the signals received from artificial Earth satellites[1]. These have shown that the amplitude of the signals may vary as the result of one or more of the following four causes: (*a*) modulation of the satellite's transmitter; (*b*) rotation of the satellite antenna relative to the receiving antenna; (*c*) Faraday fading; (*d*) fading resulting from propagation through an irregular ionosphere. Suitable instrumentation can usually remove the results of cause (*a*), while causes (*b*) and (*c*) together give rise to a regular fading component with a period of several seconds[2] and can thus be recognized easily. The rapid and random fading is attributed to irregularities in the ionosphere, much the same mechanism being involved as is considered to be associated with the scintillation of radio stars.

Radio-star scintillations have been shown to be due to the passage of the radiation from the extra-terrestrial source through an ionosphere which has clouds of enhanced ionization embedded in it[3]. Further, these clouds have been shown to have dimensions of the order of a kilometre and to be elongated along the direction of the Earth's magnetic field[4]. There is considerable evidence, from ground-based radar investigations[5] of the ionosphere, which also points to the existence of such field-aligned irregularities. Recently, Rush and Colin[6] have considered the effect this anisotropy of the irregularities has on their ability to produce scintillations. They came to the conclusion that for propagation approximately along the field lines the scintillation activity normally associated with irregular diffraction by the irregular medium should be increased because of the possibility of radiation which traverses two completely different paths reaching the receiver. The first of these paths is the direct one; the second is via grazing reflexion from the field-aligned irregularities. The geometry which they considered applies to parallel radiation from an extra-terrestrial source, but a similar effect would be expected to occur when the source is rather closer to the Earth's surface.

Observations of the radio transmissions of satellite 1959 Iota-1 (*Explorer VII*) made at Brisbane (dip, 57°) during the months of July, August and September 1960, have been analysed in an attempt to establish the existence of this effect. The satellite takes approximately 8 min. to pass over the station and a scintillation index (fading amplitude/mean level) determined from the random fading component was allotted to each half minute of this period. From the known elements of the orbit it was possible to calculate, for each traverse, the time when the satellite passed through the observer's magnetic meridian plane. The scintillation index for the ½-min. containing this time was then normalized according to the

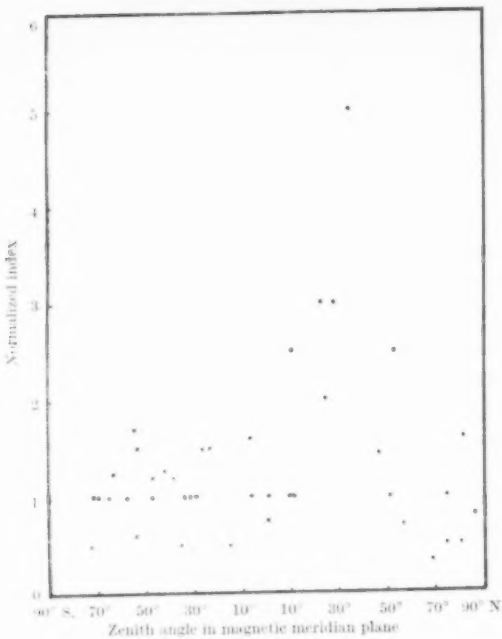

Fig. 1

general level of the scintillation index over the whole traverse. This was done to remove the diurnal and seasonal variations of scintillation activity.

A plot of the normalized scintillation index versus the zenith angle of the satellite as it passes through the magnetic meridian plane is shown in Fig. 1. If the scintillation activity is independent of the direction of propagation through the ionosphere, the points on this plot should be randomly distributed about a horizontal line, corresponding to a normalized index of one. While this is found to be generally true, the normalized index increases markedly over the range of zenith angles of 10°–55° to the north, being a maximum of 5 at 33°. This value of zenith angle in the magnetic-meridian plane corresponds to propagation along the field lines. The mean normalized index of the set of points in Fig. 1 is 1·33 with a standard deviation of 0·87. Consequently the observation at 33° is four standard deviations removed from the mean and thus constitutes an event, the probability of the occurrence of which by chance is 1 in 10^4. The two points corresponding to a normalized index of 3 are two standard deviations away from the mean, and the probability of their being chance events is 1 in 50.

Increases in scintillation index are occasionally observed when the satellite is at points outside the magnetic meridian plane. An analysis of all index increases above the general level has therefore been made to see if the increases associated with propagation approximately along the field lines are any different from the others. The number of increases for the various values of normalized index are listed in Table 1. Two of the three occasions when the normalized index is between 3 and 3·4 correspond to propagation approximately along the field lines, while the event corresponding to a normalized index of 5 corresponds to propagation exactly along the field lines. Thus the interesting points in Fig. 1 involving zenith angles 10°–50° to the magnetic north correspond to larger increases in scintillation index than observed for other directions.

Table 1

Normalized index	2·2–2·4	2·5–2·9	3·–3·4	3·5–3·9	4·–4·4	4·5–4·9	5·–5·4
No. of increases	13	6	3				1

It should also be pointed out here that no evidence of a change in scintillation-rate was found to be associated with propagation along the field lines.

While this evidence is somewhat fragmentary it would appear that the scintillation activity associated with propagation along the lines of the Earth's magnetic field is more pronounced than scintillation activity associated with other directions of propagation through the ionosphere. This result supports the suggestion of Rush and Colin[6] that other workers in this field should examine observations already made in order to verify the existence of this effect, which may prove to be a valuable tool in the study of the form of ionospheric irregularities.

Work on this and other aspects of the association of the scintillation of satellite signals with ionospheric irregularities is proceeding and will be reported more fully elsewhere.

This work has been sponsored by the Electronics Research Directorate of the Air Force Cambridge Research Center, Air Research and Development Command, under contract No. AF 64(500)–9.

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HYDROMAGNETICS AND STELLAR STRUCTURE

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IT is generally agreed that the microscopic processes of absorption and emission of electromagnetic radiation play a part in determining the macroscopic structure of gaseous stars. Thus the equation of hydrostatic equilibrium of a spherically symmetrical distribution of matter in radiative equilibrium is[1]:

$$\frac{\mathrm{d}}{\mathrm{d}R}(p_g + p_r) = -\frac{GM(R)\rho}{R^2} \qquad (1)$$

where p_g is the gas pressure, p_r the radiation pressure, G the universal constant of gravitation, $M(R)$ the mass internal to radius R, and ρ the density.

Now the emission and absorption of hydromagnetic radiation is a process usually on a macroscopic scale, and therefore will play a part in determining the structure of magnetic stars on a larger scale. Thus in determining equilibrium structure on this large scale, the radiation pressure in equation (1) should be written as the sum of electromagnetic radiation pressure and hydromagnetic radiation pressure. (In the absence of a magnetic field model, the latter is here assumed to be isotropic.) That is :

$$p_r = p_{er} + p_{hr} \tag{2}$$

Let us consider, for example, the special case of the Sun. It is thought[2] that many features visible on the solar disk (for example, sunspots, flares, prominences) are manifestations of magnetic energy transmitted outwards from the Sun's inner regions. Further, movements and structure in the inner solar corona suggest that hydromagnetic energy may be both absorbed and generated there. Certainly solar-generated magnetic disturbance is observed at the Earth, suggesting that the Sun is luminous at hydromagnetic frequencies. Yet the Sun in all its visible parts preserves a gross constancy of structure. These things may be reconcilable through the concept of gross equilibrium under the influence of not only electromagnetic but also hydromagnetic radiation pressure. This is embodied in equations (1) and (2).

In the interior of the Sun p_{er} and p_{hr} may be of comparable importance. In the solar corona, however, p_{hr} should dominate. (Available data suggest that radiation pressures in optical and radio frequencies have negligible effects on gross movement in the corona.) Thus on the assumption of gross hydrostatic equilibrium the description of the solar corona (considered to be permeated with magnetic field (H)) under hydromagnetic radiative equilibrium is given by :

$$\frac{\mathrm{d}}{\mathrm{d}R}(p_g + p_{hr}) = -\frac{GM(R)\rho}{R^2} \tag{3}$$

By analogy with the theory of electromagnetic radiative equilibrium :

$$\frac{\mathrm{d}p_{hr}}{\mathrm{d}R} = -\frac{K_h L(R)\rho}{4\pi V_A R^2} \tag{4}$$

and

$$\mathrm{d}L(R) = 4\pi R^2 \rho \varepsilon_h \mathrm{d}R \tag{5}$$

where : $L(R)$ = flux of hydromagnetic energy through concentric sphere of radius R ; K_h = coefficient of hydromagnetic opacity ; $V_A = H/\sqrt{4\pi\rho}$, the Alfvén speed ; ε_h = hydromagnetic emissivity per unit mass.

The equation (3) differs from that of Chapman[3] and Parker[4] for hydrostatic equilibrium in the solar corona which is :

$$\frac{\mathrm{d}p_g}{\mathrm{d}R} = -\frac{GM(R)\rho}{R^2} \tag{6}$$

Because of the nature of the solution of equation (6), Parker was led to the belief that the solar corona is expanding subject to the equation :

$$\rho v \frac{\mathrm{d}v}{\mathrm{d}R} = -\frac{\mathrm{d}p_g}{\mathrm{d}R} - \frac{GM(R)\rho}{R^2} \tag{7}$$

Equations (3) and (7) have one feature in common, namely, that they both imply a radial flux of momentum. Equation (7) implies in addition the radial movement of matter. It would seem that equation (3) offers a solution to the difficulties inherent in the solution of equation (6) without recourse to equation (7).

Quantitative argument against the use of equation (7) to describe the solar corona is as follows. First, it neglects altogether the effect of magnetic fields close to the Sun (say, within 2 solar radii) on any attempted expansion. This can only be justified if the kinetic energy density is very much greater than the magnetic energy density there. Assuming a density at the base of the corona of 2×10^8 protons per cm.^{3} and an outward velocity of 100 km./sec. the former is about 10^{-2} ergs per cm.^{3}. Such an energy density is exceeded by magnetic field of only one gauss. Larger fields than this may abound in the lower corona (cf. ref. 5). Parker considers magnetic fields only in the regions of interplanetary space where their energy density is already negligible compared to the kinetic energy density predicted by his model. Thus magnetic fields at the base of the corona may inhibit the expansion attributed to it.

Secondly, the inner corona is known to contain magnetic fields and to manifest movements which are not well correlated throughout the whole region. Let us delineate this inner region by a sphere D (of radius α) concentric with the Sun. α may be a few solar radii. Let us suppose that hydromagnetic waves are generated at the surface of D and emitted outwards into the surrounding medium which is traversed either by the solar magnetic field or an interplanetary field. The outward flow of momentum due to such emission could cause sufficient reaction on D to inhibit its expansion. Thus (if α is 2 solar radii) $2{\cdot}8 \times 10^6$ protons per cm.^{3} there[6], moving outward at 100 km./sec., would represent an outward momentum flux of about 10^{-4} erg/cm.^{3} at the surface of D. This may be inhibited by the reaction to outwardly propagated hydromagnetic waves for which the flux of momentum (F) is given by $\frac{(\Delta H)^2}{8\pi}\frac{V_A^2}{c^2}$, where ΔH is the disturbance magnetic field. Putting $H = 10$ gauss and $\Delta H = 1$ gauss, $F \approx 10^{-4}$ erg/cm.^{3} on the surface of D. Of course, such hydromagnetic radiation reaction would occur in a continuous fashion all through the inner corona and may inhibit altogether the expansion of the solar corona which is inevitable on Parker's model.

In view of these criticisms, I consider it is not proved that outstreaming of coronal gas to distances of astronomical units[4] is a general condition of the Sun. However, the generation of outward-travelling hydromagnetic waves in the inner corona would seem to be an inevitable consequence of the interaction of momentum and magnetic fields there, both of which are observed to be of the utmost complexity. Moreover these waves, the wave-lengths of which may exceed the dimensions of the Earth, can cause corpuscular bombardment of the Earth and comets. A theory of solar-generated geomagnetic disturbance and auroras based on the propagation of hydromagnetic waves all the way from the Sun has been initiated earlier[7–10].

An experimental test to decide between Parker's expansion model[4] and the above hydromagnetic model of the solar corona may be provided by

observation of hydrogen spectra in the night glow. On Parker's model one would expect a permanent red Doppler shift in H_α of about 10 Å., while on the hydromagnetic model one would expect only Doppler broadening of variable amounts. Shklovsky[11] reports that Prokudina's observations of H_α in the night glow showed a Doppler broadening of no more than 2 Å. However, the observation should be repeated with a design to distinguish the above two models. Of course, the contribution to hydrogen line intensities by the geocorona would have to be eliminated perhaps by a space-probe or satellite experiment.

The establishment of the usefulness of equation (3) in studying the solar corona would be strong support for the incorporation of equation (2) in the study of stellar structure in general.

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INTESTINAL ABSORPTION OF VITAMIN B_{12} AND OF A VITAMIN B_{12}-PEPTIDE COMPLEX IN NORMAL SUBJECTS AND IN PATIENTS WITH PARTIAL GASTRECTOMY

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THE partially gastrectomized patient seemed to provide adequate conditions to elaborate a test for the detection of minor impairment in intestinal vitamin B_{12} absorption, as well as to compare the absorbability of different vitamin B_{12} preparations.

Work on the behaviour of partially gastrectomized patients has led to conflicting results. Glass *et al.*[1], using surface scintillation counting of the liver after oral administration of the radioactive vitamin[2], found a decrease in radioactivity uptake by the liver in 7 out of 8 patients. More recently, Brodin *et al.*[3], using the Schilling test[4], reported a normal urinary excretion of radioactive vitamin B_{12} in 30 patients; only 4 patients had low excretion values. This would indicate the existence of a minor impairment, which I wished to demonstrate clearly. Furthermore, I compared the absorption, in normal patients as well as in partially gastrectomized patients, of crystalline vitamin B_{12} and of the vitamin B_{12}-peptide complex, isolated from a microbial fermentation.

The radioactive test had therefore to be modified to enable me to measure the amount of vitamin B_{12} absorbed by the intestine after the ingestion of a dose large enough to saturate the absorption system, for example, 10 μgm. This dose is present in a normal diet, and is certainly too small to involve a diffusion mechanism during the absorption process, which has been postulated to explain the absorption after feeding with large oral doses.

Labelled vitamin B_{12} is obtained from a culture of *Propionibacterium freudenreichii* in a medium containing cobalt-60. The labelled vitamin B_{12}-peptide complex is prepared by exchange in an acid medium with unlabelled peptide complex or by addition of the labelled vitamin B_{12} to a solution of the peptide.

1 μgm. of labelled vitamin is injected intravenously into the patient and the surface counting of the liver is recorded with a scintillation counter 2, 4, 6 days afterwards. During this time-interval, there is no appreciable excretion of radioactivity and the surface counting of the liver remains practically constant from the fourth to the thirtieth day. This measurement is used as a standard for the calculation of the amount of vitamin B_{12} or vitamin B_{12}-peptide absorbed by the intestine after oral administration. Then a known amount of vitamin B_{12} of given specific radioactivity is given by mouth and a new surface counting is made. The counts corresponding to each administration add to the previous counting.

The amount of absorbed vitamin B_{12} is given by the formula:

$$\underset{(\mu\text{gm.})}{x} = \frac{N - n}{n} \cdot \frac{R_s}{r_s} \qquad \text{(I)}$$

where N is surface counting of the liver after the oral dose, n is surface counting of the liver after intravenous injection, R_s is specific radioactivity of the injected vitamin B_{12}, r_s is specific radioactivity of the ingested vitamin B_{12}.

The percentage absorption is equal to $\frac{x}{a} \times 100$ (II),

where a is oral dose of vitamin B_{12} in μgm.

To estimate intestinal absorption, Glass[1,2] measures the liver radioactivity after an oral dose of 0·5–1 μgm. of labelled vitamin B_{12} and he expresses the results in counts/min. over the abdominal background. If he gives the amount of vitamin B_{12} absorbed, he uses formula (I), where N and n are equal to the surface counting of the liver diminished from the surface counting of the spleen, as some radioactivity is uniformly spread over the abdomen.

From Fig. 1, it is clear that the counting over the liver (A) includes the liver radioactivity plus the radioactivity of the abdomen; furthermore, the surface counting of the spleen (B) includes also some of the radioactivity present in A. The importance of this additional radioactivity can be assessed by a third measurement at C, which is symmetrical to B

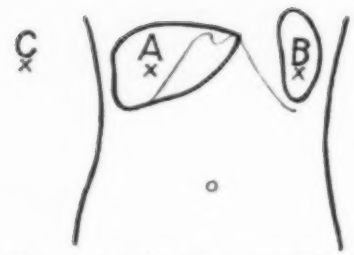

Fig. 1. Schematic representation of the abdominal projection of the liver and spleen

in respect to A and where the additional radioactivity originating from A is the same as at B. The radioactivity of the liver surface is, therefore:

$$N = N_1 - (N_2 - N_3),$$

where N_1 is radioactivity at A, N_2 is radioactivity at B, N_3 is radioactivity at C.

Experimentally, N_3 is of the order of 15 per cent of N_1.

(1) *Normal subjects.* Table 1 gives the results relative to the amount of vitamin B_{12} absorbed after an oral dose of 10 μgm.

Table 1. Absorption of Vitamin B_{12} in Normal Subjects

Case	Sex	Age (yr.)	Absorption (μgm.)
1	F	82	2·5
2	M	44	4
3	M	35	5
4	M	55	4·2
			Mean 3·9

Therefore, under normal conditions, about 4 μgm. of vitamin B_{12} are absorbed after an oral dose of 10 μgm. This amount is higher than that found by Glass[5]; according to him, the amount of absorbed vitamin B_{12} is about 1 μgm. for oral doses varying from 2 to 50 μgm. My results agree with that of Reizenstein and Nyberg[6], who found $3 \pm 0{\cdot}9$ μgm. of vitamin B_{12} retained after ingestions varying from 4 to 50 μgm.

(2) *Partially gastrectomized patients.* The results concerning 5 patients are reported in Table 2.

The intestinal absorption of vitamin B_{12} is well below normal in partially gastrectomized patients (45 per cent of the amount absorbed by the normal subject).

(3) *Absorption of a vitamin B_{12}-peptide complex.* I gave orally an amount of the labelled vitamin B_{12}-peptide complex equivalent to 10 μgm. of vitamin B_{12} to the same normal subjects as well as to the same partially gastrectomized patients. The results are shown in Table 3 in μgm. of vitamin B_{12} absorbed.

Table 2. Absorption of Vitamin B_{12} in Partially Gastrectomized Patients

Case	Sex	Age (yr.)	Absorption (μgm.)
5	M	66	2·1
6	F	44	2·7
7	M	65	1·4
8	M	50	1·0
9	M	69	1·5
			Mean 1·8

Table 3. Absorption of the Vitamin B_{12}-Peptide Complex

Case	Normal subjects Absorption (μgm.)	Case	Partially gastrectomized patients Absorption (μgm.)
1	2·65	5	4·7
2	4	6	3·2
3	6·5	7	3·8
4	3·7	8	2·2
		9	4·7
	Mean 4·2		Mean 3·6

From Table 3, it is apparent that in the normal subject there is no difference in absorption between the vitamin B_{12}-peptide complex and vitamin B_{12} itself. In the partially gastrectomized patients, intestinal absorption of the vitamin B_{12}-peptide is twice as high as that of vitamin B_{12} and the quantity absorbed has reverted to normal values.

It is thus shown, using adequate testing conditions (10 μgm. of labelled vitamin B_{12} for the oral dose and a modified surface liver counting), that intestinal absorption of vitamin B_{12} is impaired in the partially gastrectomized patient. The vitamin B_{12}-peptide complex, isolated by Heathcote and Mooney[7], can restore completely the absorption. According to these findings, the partially gastrectomized patient is well suited to test the factors involved in vitamin B_{12} absorption.

I am indebted to Dr. Heathcote for the vitamin B_{12}-peptide complex.

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RETINAL CORRESPONDENCY AND THE HOROPTER IN ANOMALOUS CORRESPONDENCE

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VISUAL direction is of particular interest because of its remarkable delicacy and its important contribution to space perception. It rests primarily on the organization of the retinas one to the other, and both to that of the visual cortex. With continuous bifixation on a small object, it is possible to position in space a number of object-points (conventionally in a horizontal plane) such that each is seen in the same direction from the observer when viewed alternately by the eyes. This group of points constitutes one type of empirical horopter, the identical-

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visual-direction horopter. Study of the horopter curve has led to greater understanding of the normal organization of corresponding areas between the two retinas. In this system the centres of the two foveas correspond; moreover, one eye's temporal retinal elements (connecting neuroanatomically with cells in the ipsilateral occipital cortex) correspond with nasal retinal elements of the other eye (which connect with cortical cells in the same hemisphere).

But the nature of anomalous retinal correspondence remains an enigma. In this form of retinal correspondence, found in many persons with strabismus ('crossed eye'), the two foveas do not correspond: instead, the fovea of one eye functionally corresponds with an extra-foveal point in the other retina. Thus, there is the curious implication that pairs of corresponding retinal points can be associated between opposite occipital hemispheres. With anomalous correspondence in esotropia, for example, certain retinal points nasal to the fovea of a deviated (right) eye and connecting with the contralateral (left) occipital cortex would be functionally corresponding with nasal retinal elements of the other eye which lead to the contralateral (right) cortex. Whether there can be correspondence between opposite occipital hemispheres depends on whether there is a horopter in anomalous retinal correspondence.

Verhoeff[1] claims there is no retinal correspondency in anomalous correspondence. However, most experimentalists intuitively believe that a horopter should be demonstrable. Although there has been an occasional paper discussing the matter, we have been unable to learn of an investigation in which the horopter has been demonstrated in anomalous correspondence. Halldén[2], who succeeded in obtaining a two-point horopter in the course of studying another feature of anomalous correspondence, noted that, " . . . in cases of anomalous correspondence investigation of the horopter is attended by very considerable difficulties". Ogle[3], who has probably had more experience with the horopter than any other researcher, remarked on the horopter in subjects with strabismus, " . . . my experience is a most frustrating one: the subjects are so indefinite as to what or how they see . . .". In spite of a lack of published reports, the indication is that investigations have been attempted, but without success.

After several years work we have been able to obtain the empirical longitudinal horopter in anomalous correspondence[4]. In this first article we wish to report only on the experimental procedure and method of analysis which we have found to be applicable in either strabismus or normal binocular vision.

The criterion of identical visual direction is used. The apparatus (Fig. 1) consists of a frame arranged in a frontoparallel plane which may be used at fixation distances of 75 cm.–6 m. An upper section contains several vertically oriented 'Plexiglass' rods which may be placed as much as 75 cm. to either side of the central fixation point: a lower section contains a cable and scale about 3 m. in length along which a mobile rod may be moved by the observer. The rods (¼ in. diam., 9 in. long) are painted on one end and on the side opposite the observer. A 2·2-V., 0·25-amp. 'bullseye' bulb is placed in contact with the unpainted end of each rod. The lower mobile rod and a selected fixed rod above are alternatively illuminated at a rate adjusted for vivid perception of apparent movement (2–4 c.p.s.). Fixation is continuously maintained on a central red spot (2 mm. diam.) that is optically imaged in the middle of a ¼-in. gap between the upper and lower rods. A large sheet of 'Polaroid' filter (*HN* 34 linear polarizer) is placed with axis 45° in front of the upper rods; another sheet with axis 135° is placed before the lower rod. The head is fixed by means of a mouth-bite. 'Polaroid' filters appropriately oriented before the eyes make an illuminated upper rod visible only to the fixating (dominant) eye and the lower rod visible only to its fellow. While fixating the central red spot, the observer moves the lower rod by means of a pair of synchronous ('Selsyn') motors until the apparent movement between the alternately illuminated rods is purely vertical (that is, no lateral component in the movement is seen). The identical-visual-direction setting is greatly aided by the appearance at this point of a unique 'pouring effect' or 'piston effect'. The position of the lower rod with respect to the fixation point is read from a scale behind the rod holder.

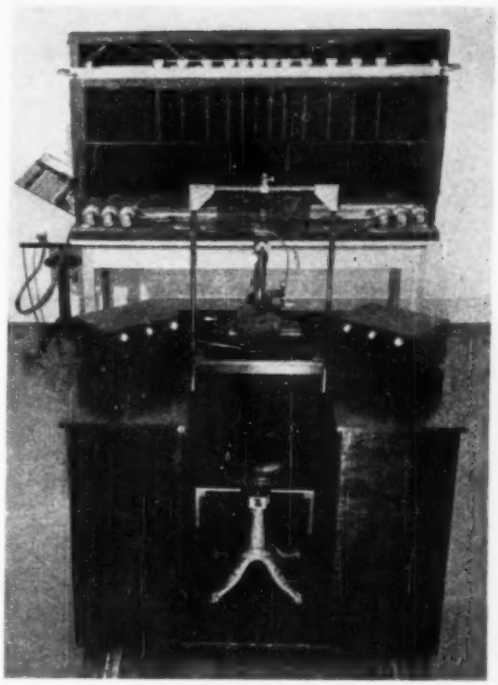

Fig. 1. The horopter apparatus

The mean setting of the lower mobile rod together with the position of the corresponding upper rod specifies a point on the horopter that lies in the visual plane. In a system of rectangular co-ordinates with the origin at the mid-point between the entrance pupil centres, x equals $a(T_L + T_R)/(2a + T_L - T_R)$ (Eq. 1), and y equals $2ab/(2a + T_L - T_R)$ (Eq. 2) where $2a$ is the interpupillary distance, b is the fixation distance, and T_L and T_R are the rod settings for the left and right eyes, respectively. The aggregate of the spatial points for which data have been obtained gives the empirical identical-visual-direction horopter.

The longitudinal angles α_L and α_R subtended respectively at the left and right eyes by the fixation point and one horopter point are obtained from the equations: $\tan\alpha_L = bT_L/(b^2 + a^2 + aT_L) = (bx - ay + ab)/(ax + by + a^2)$ (Eq. 3), and $\tan\alpha_R = bT_R/(b^2 + a^2 - aT_R) = (bx + ay - ab)/(-ax + by + a^2)$ (Eq. 4).

Ogle[5,6] has shown that for subjects with normal binocular vision the empirical horopter is satisfactorily described by a conic the skew of which, R_0, and curvature, H, at the fixation point are obtained from an analytical plot of data which are fitted to the equation $\tan\alpha_R/\tan\alpha_L = R_0 + H\tan\alpha_R$ (Eq. 5). For simplicity Ogle's mathematical model is based on the assumption that the angular separation between the fixation point and a central point on the horopter would be small compared with angle α, and that the fixation disparity responsible for this would be equal in the two eyes. We have found Ogle's model applicable in normal binocular vision, but quite inadequate for analysis of the horopter in strabismus. This is not surprising since the horopter in strabismus should be expected often to miss the fixation point by a rather large angular amount (equivalent to the 'subjective angle'). In fact, in strabismus with normal correspondence the horopter should (and our experiments indicate that it does) pass through the point of intersection of the visual axes. For this reason, as well as the fact that in strabismus the 'turning' is not equal in the two eyes but rather is confined to one eye (at a time), it became apparent to us that a new mathematical model was needed for analysis of the horopter in strabismus.

Our mathematical model includes a constant F which denotes the tangent of the angular displacement of the horopter from the fixation point, a constant M which denotes the skew of the horopter with respect to an objective fronto-parallel plane of the observer, and a constant C which denotes the curvature of the horopter where it crosses the visual axis of the fixating eye. The equation which relates these constants in a form comparable to Ogle's[6] is $U = \tan\alpha_m/\tan\alpha_f = (F/\tan\alpha_f) + M + C\ \tan\alpha_f$ (Eq. 6), where α_f is the longitudinal angle subtended at the fixating or dominant eye by the fixed rod and the fixation point, and α_m is the corresponding angle subtended at the other eye by the mobile rod and the fixation point. F is zero when the horopter passes through the fixation point; it is positive for eso- and negative for exo-fixation disparity when the right eye is fixating, and the reverse for left eye fixation. M is a measure of the relative magnification of the images in the two eyes. When M is greater than unity, the image is larger for the eye viewing the fixed rods; when less than unity, the image for this eye is the smaller. C represents the deviation of the empirical horopter from the theoretical curve that would result from all longitudinal angles being equal. With exact bifixation, this theoretical curve is the Vieth-Müller circle and the deviation of the empirical horopter from it is the Hering-Hillebrand deviation. The constant C is a measure of the relative asymmetry in the distribution of corresponding retinal points in the two eyes. With the right eye fixating, C is positive when the horopter has greater curvature than the theoretical curve, and negative when it has less curvature than the theoretical curve, or when it is convex toward the eyes; with left eye fixation the signs are reversed.

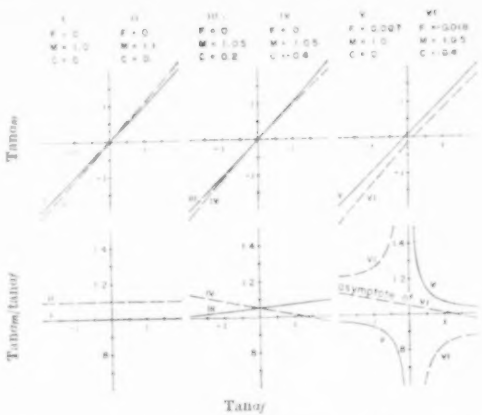

Fig. 2. Bottom, plot of $\tan\alpha_m/\tan\alpha_f = (F/\tan\alpha_f) + M + C\ \tan\alpha_f$ is comparable to Ogle's (refs. 5 and 6) well-known analysis of horopter data. Simple transformation gives $\tan\alpha_m = F + M\ \tan\alpha_f + C\ \tan^2\alpha_f$ (top). The constants F (displacement of horopter from fixation point), M (horopter skew), and C (horopter curvature) are the same in both plots

When F is not zero the plot of Eq. 6 is a hyperbola (Fig. 2, bottom), one asymptote being essentially the ordinate axis, the second asymptote being a straight line with the formula $U = M + C\ \tan\alpha_f$ (Eq. 7). This straight line becomes the entire curve (a degenerate hyperbola) when F equals zero. In either case the slope of this line gives the curvature of the horopter and M, the ordinate intercept, gives its skew. The hyperbola becomes asymptotic to the ordinate axis in quadrants I and III when F is positive, and II and IV when F is negative. The larger the absolute value of F, the greater is the eccentricity of the hyperbola.

To solve for the constants F, M and C, we have found it more convenient to use the transformed equation (Eq. 8) $\tan\alpha_m = F + M\ \tan\alpha_f + C\ \tan^2\alpha_f$. The plot of this equation is a parabola (Fig. 2, top). In this plot, F is the ordinate intercept, M is the slope, and C represents the curvature.

In our model the equation for the spatial plot of the horopter is a third-order polynomial in x and y which is difficult to use in fitting a curve to the data. It is simpler to use instead a pair of parametric equations.

The present experimental apparatus and mathematical analysis may be applied to a wider range of ocular conditions than was formerly possible, yielding comparable constants for the horopter in normal binocular vision, strabismus, and anomalous retinal correspondence. The functional relationship between the two retinas in anomalous correspondence will be reported in a subsequent communication.

This investigation was supported in part by a research grant (No. B-2442) from the National Institute of Neurological Diseases and Blindness, U.S. Public Health Service.

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EFFECT OF CORTISONE AND RELATED COMPOUNDS ON THE BIOGENESIS OF CARTILAGE

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ADMINISTRATION of cortisone to whole animals has been shown to produce the following effects in connective tissue, including bone and cartilage: (1) Reduction in the metachromatic staining of the 'ground substances', mast cells and matrix of bone and cartilage. (2) Reduced uptake of radiosulphate ($^{35}SO_4^{2-}$) by connective tissues. These investigations, primarily associated with the names of Layton, Dziewiatkowski, Schiller and Asboe-Hansen, have been reviewed recently[1].

It must be stressed that such effects (and those described in this article) are only obtained with relatively high (pharmacological) doses of cortisone and are probably of little physiological significance. They assume greater significance when considered in relation to the undesirable side reactions attending the clinical use of cortisone, hydrocortisone and more potent chemical modifications of these hormones, as anti-inflammatory agents and for treatment of the 'collagen diseases'.

Since connective tissue is rich in mucopolysaccharide sulphates (heparin, chondroitin sulphates, keratosulphate, heparitin sulphates, etc.), it is generally concluded that cortisone depresses the overall production of sulphated polysaccharides in these tissues. This conclusion is scarcely justified by the above evidence alone, concerned as it is only with the metabolism of the sulphate groups (responsible for the metachromasia) of the connective tissue polysaccharides.

Boström and his co-workers[2,3] found that addition of cortisone depressed the incorporation of radiosulphate into slices of costal cartilage suspended in a Krebs–Ringer solution. Under these conditions and in the absence of added glucose and amino-acids, there was no significant synthesis of the polymeric components of cartilage. Boström concluded that cortisone reduced the activity of an enzyme reaction which promoted an exchange between the sulphate groups of the cartilage polysaccharides and the inorganic radiosulphate of the medium.

Other investigations[4] have indicated that cortisone has little effect on sulphate metabolism in the mucin-secreting cells of the gastro-intestinal tract. The mucins formed here contain ester sulphate, associated with the viscous polymeric constituents (mucosubstances). Once synthesized, the mucins are extruded into the gut and, being extracellular, are unlikely to enter into further enzymic exchange reactions with inorganic sulphate. By contrast the polymeric ester sulphates contained in connective tissues, though extracellular, are in more intimate association with the enzymes of cells than are components of extruded mucins. They are thus able to participate in sulphate exchange reactions which may be sensitive to cortisone.

We have now studied the effects of a number of steroid hormones and drugs which exhibit glucocorticoid and anti-inflammatory activities on the biogenesis of cartilage in tissue culture. For comparison, we also observed the effects of some non-steroid anti-flammatory agents upon this system *in vitro*.

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Advantages of Tissue Culture

Under suitable conditions, cartilage may be induced to form *de novo* from chick embryonic somites[5]. Using this system, it is possible to study biogenesis of cartilage and its constituents[6]. Cartilage begins to form on the fourth day of culture, following induction. Measurements made at this time and in the subsequent three days primarily record the biogenesis of the cartilage constituents rather than any 'turn-over' of such constituents. Whole animal studies or *in vitro* studies with excised tissues from other than early embryonic sources usually record the sum of the synthetic and degradative processes. The biogenesis of a tissue component may be distinguished, however, from any subsequent turnover when it is first formed *de novo*, as in early stages of tissue cultures which are undergoing morphological and biochemical differentiation.

A further advantage of tissue culture studies is that topical effects of an applied drug or hormone may be readily observed. Such effects will not normally be the consequences of metabolism of the active principle or of mediation through other principles (for example, pituitary-adrenal axis), as they might be *in vivo*. Furthermore, any effects observed will probably be due to the actual concentration of drug or hormone present, added in known amounts to the tissue cultures. Losses and dilutions due to elimination, catabolism or storage in extracellular compartments will be reduced to an experimental minimum.

Methods

Three-day-old chick embryonic somites, when excised and placed in culture, form primarily mesenchymal tissues. If cultured in the presence of spinal cord or notochord, however, nodules of hyaline cartilage are formed[5].

Cartilage formation was therefore induced by placing somites and notochord together on lens paper floating above 1 ml. of nutrient medium (horse serum-embryo extract-balanced salt solution) which also contained $Na_2{}^{35}SO_4$ (5 microcuries)[6]. Added steroids (final concentration, $1{\cdot}5 \times 10^{-4}$ *M*) were emulsified with polyoxyethylene sorbitan monolaurate ('Tween 20'). Equivalent amounts of 'Tween' (800 µgm./ml.) were added to the control cultures. A minimum of ten cultures with each drug or hormone and ten control cultures were set up simultaneously. All cultures were maintained in a humid atmosphere at 37° C. for 6–8 days. The formed cartilage was removed and extracted successively with potassium chloride (made alkaline with potassium carbonate) and then with dilute potassium hydroxide. These extracts contain more than 90 per cent of the chondroitin sulphate present in the cartilage. Little or no keratosulphate was synthesized by this newly formed cartilage[6]. Sulphate ions were

Fig. 1. Paper ionophoresis of metachromatic polysaccharides: (*a*) from normal cultures; (*b*) from cultures grown in the presence of hydrocortisone (10^{-4} *M*); (*c*) chondroitin prepared by chemical desulphation of chondroitin sulphate *A*; (*d*) chondroitin sulphate(s) extracted from bovine trachea. (Ionophoresis at 23° on Whatman 3 *MM* paper 0·2 *M* sodium borate, *p*H 8·6, 4 hr., with potential gradient of 12 V./cm. Metachromasia was detected by immersion in 0·15 per cent (w/v) thionine in 65 per cent (v/v) ethanol, acidified with 0·1 per cent (v/v) acetic acid. Excess stain was removed with 95 per cent ethanol)

removed by prolonged dialysis of the extracts, after the additions of non-radioactive sodium sulphate. Aliquots were dried, and incorporated sulphur-35 measured by direct counting. The uronic acid content of these dialysed extracts was measured colorimetrically using the carbazole-sulphuric acid reactions[7]. Full experimental details have been given elsewhere[6].

Results with Cortisone and Hydrocortisone

Both these hormones severely depressed the growth of cartilage as observed microscopically. The uptake of radiosulphate into the chondroitin sulphate fraction was also much reduced. However, the amount of non-dialysable uronic acid found in extracts from cartilage grown in the presence of these hormones was not significantly less than that present in extracts of the control cultures (Table 1).

When extracts from the cortisone and hydrocortisone-treated cultures were examined by paper ionophoresis (Fig. 1) it was found that the principal metachromatic component had a lower ionophoretic mobility than mixtures of chondroitin sulphates *A* and *C* extracted from animal cartilage (bovine nasal septa, trachea, chicken costal cartilage, elasmobranch endoskeleton, etc.), but corresponded in mobility to a chemically desulphated[8] preparation of chondroitin sulphate *A* (containing about 2 per cent residual ester sulphate). Extracts from control cultures contained as their principal metachromatic components, chondroitin sulphate(s) with ionophoretic mobilities almost identical with authentic specimens from animal cartilage (15 per cent ester sulphate).

These analytical findings suggest that cortisone and hydrocortisone do not primarily affect the biosynthesis of the polysaccharide portion (chondroitin) of the chondroitin sulphate (containing glucuronic acid and N-acetylgalactosamine) but that they do influence its subsequent sulphation.

Table 1. Effect of some Hormones and Drugs on (*a*) the Incorporation of Radiosulphate into Chondroitin Sulphates (*a*) and on (*b*) the Non-dialysable Uronic Acid Fraction extracted from Cartilage formed *de novo* in Tissue Culture

Compound (final conc. added) $1·5 \times 10^{-4}$ *M*	No. of cultures	Uronic acid content	$^{35}SO_4^{2-}$ incorporated
None	2 × 10	100*	100*
Hydrocortisone	5 × 10	100	27
	20	120	19
Cortisone	5 × 10	100	28
Progesterone	2 × 10	100	100
Testosterone	10	100	100
Deoxycorticosterone	20		100
Prednisone	10		26
Prednisolone	3 × 10	80	0

* Controls were assigned a value of 100.

The deoxyribonucleic acid contents of both the cultures treated with hydrocortisone (or prednisone) and of the control cultures increased by only 30 per cent during the period required for cartilage-formation. The effects of hydrocortisone cannot therefore be explained simply as an inhibition of cell multiplication and loss of viability during this period. This was also directly demonstrated by experiments in which somites and notochord were exposed to hydrocortisone for various intervals less than the four days required for the appearance of normal cartilage in control cultures. When the tissues were afterwards transferred to hydrocortisone-free growth medium, they recovered their capacity to make normal cartilage, took up radiosulphate and formed metachromatic material with the same ionophoretic mobility as chondroitin sulphate.

The following considerations would seem to eliminate one further explanation of our analytical results, namely, that the steroid hormones are activating an enzyme system (chondrosulphatase) which removes ester sulphate from initially formed chondroitin sulphates. Though sought, such a chondrosulphatase has never been described in mammals. Chondrosulphatases have only been reported to be present in some bacteria and certain molluscs[9,10]. When normal cultures were grown in the radiosulphate medium for 5–8 days and afterwards transferred to a medium containing no $^{35}SO_4^{2-}$, the rate of loss of incorporated radioactivity due to subsequent turnover and exchange of the ester sulphate groups was not affected by the presence of cortisone or hydrocortisone in this second medium. The result seems to exclude an activation of any chondrosulphatase enzymes present in the cartilage cultures by these steroids.

Adrenocorticotrophic hormone had no effect on cartilage formation in this system, as might be expected if it is the adrenal corticoids themselves which are pharmacologically active. Other steroid hormones (deoxycorticosterone, progesterone, testosterone, corticosterone) were without measurable effect on chondrogenesis.

Results with Some Synthetic Glucocorticoids

The following compounds were tested: prednisone (Δ^1-cortisone) and prednisolone (Δ^1-hydrocortisone) (Merck, Sharp and Dohme); the 6α-methyl derivative of cortisone, hydrocortisone, prednisone and prednisolone (Upjohn Co.); the 9α-fluoro and 9α-fluoro, 16α-hydroxy derivatives of hydrocortisone and prednisolone (E. R. Squibb and Sons).

All these, with the exception of 6α-methylprednisolone (Medrol), depressed cartilage and chondroitin sulphate synthesis at concentrations of $1·5 \times 10^{-4}$ *M*. They were nearly all as potent as hydrocortisone. In some instances, for example, with prednisolone, 16α-hydroxy-9α-fluorohydrocortisone, they were more active as inhibitors of chondrogenesis. Their inhibitory effects generally paralleled their relative anti-inflammatory properties[11]. Insufficient determinations were made with each drug to assess accurately their relative potencies.

As with cortisone or hydrocortisone, the sulphation rather than the biosynthesis of (unsulphated) chondroitin was primarily inhibited.

Results with some Non-steroid Anti-inflammatory Agents

Potassium salicylate at high concentrations (1.5×10^{-2} *M*) greatly depressed chondrogenesis and was remarkably specific in its action. Its close chemical analogues, potassium benzoate and potassium thiosalicylate, were quite without effect at this concentration. Boström and Månsson[2] have previously reported the cortisone-like effect of salicylate on the sulphate exchange reaction in cartilage slices *in vitro*. Further analyses indicated that, as with cortisone, sulphation but not the biosynthesis of the chondroitin was chiefly affected.

Phenylbutazone and cinchophene at concentrations of 3×10^{-4} *M* had no detectable action on chondrogenesis *in vitro*.

Discussion and Conclusions

Cortisone, hydrocortisone and their chemical analogues apparently inhibit the formation of acid mucopolysaccharides in connective tissue, primarily by inhibiting the sulphation of the pre-formed polysaccharide. Hvidberg and Jensen[12] have recently shown that cortisone administration leads to loss of metachromasia and water content in the polysaccharide fraction of mouse skin. After cortisone treatment the average molecular weight of this mixture of polysaccharides was 20 per cent lower than in the controls, but the amino-sugar content was unchanged. These findings suggest that cortisone likewise inhibits sulphation, but not the synthesis, of the polysaccharide portion of polysaccharides *in vivo*. Failure to form normal amounts of the acidic macromolecule (for example, chondriotin sulphate) would in turn affect deposition and orientation of the basic collagen-like proteins of connective tissue. Other properties depending on the presence and maintenance of the acidic sulphate groups on a structural component (serving as natural cation exchanges) such as retention, deposition or movement of ions and water, would also be grossly influenced by cortisone treatment.

Recent work on the biosynthesis of chondroitin sulphates[13–15] indicates that sulphation of chondroitin only occurs at a very late stage in the overall biosynthetic sequence. Incorporation of inorganic sulphate into, and subsequent polymerization of, hexose sulphates seems to be excluded as a major biosynthetic process. Sulphate ions are activated for metabolism by reaction with adenosine triphosphate to form adenosine-3′-phosphate-5′-phosphosulphate (PAPS)[15]. PAPS is formed by extracts of costal cartilage[17], liver[15,16] and hen oviduct[14], which also contain enzymes which will transfer the sulphate group from PAPS to chondroitin and partially sulphated chondroitin[13–15]. We have failed to find any direct inhibition by hydrocortisone or prednisolone (10^{-4}*M*) of PAPS formation or of the transfer of sulphate from PAPS to phenolic acceptors by soluble enzymes from rat liver[18], intestinal mucosa or kidney[19].

The one tissue where cortisone can usefully be applied clinically to suppress inflammation, the eye, normally contains in the cornea significant amounts of unsulphated chondroitin (25 per cent of the total polysaccharides) as a structural component[20]. Is it mere coincidence that in this tissue, where inhibition of sulphation would have the least consequence, cortisone has such a beneficial effect in arresting inflammation and so little undesirable side effect? Here, there would be in essence, anti-inflammatory activity without anti-sulphation activity. This desirable end is found otherwise only with certain non-steroid drugs, for example, phenylbutazone.

We are much indebted to Dr. Karl Meyer for a sample of chondroitin and to Drs. Robert H. Levin, Mary A. Scheri, Josef Fried and John A. Bauer, for supplying the drugs mentioned. This work was supported by grants from the National Institutes of Health (U.S. Public Health Service) and the Helen Hay Whitney Foundation.

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INCREASED DIHYDROFOLATE REDUCTASE ACTIVITY AS A POSSIBLE BASIS OF DRUG RESISTANCE IN LEUKÆMIA

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LEUKÆMIC cells initially sensitive to the action of folic acid analogues develop resistance to inhibition by these drugs[1]. It has been suggested that the decreased efficacy of the antifolates may be due in part to the increased capacity of resistant cells to reduce folic acid compounds to the coenzymatically active tetrahydro-forms[2–6]. This theory is attractive since the antifolates are known to be extremely effective inhibitors of the enzyme system which catalyses the reduction of folic acid to tetrahydrofolic acid[7–10].

In the present investigation dihydrofolate reductase activity has been estimated in tissues of mice with

Table 1. Sub-lines of Mouse Lymphoid Leukæmia *L*1210 used in this Work

All sub-lines were carried in hybrid male mice (*BALB/c An* × *DBA/2J*) F_1. (Referred to commonly as *CDBA*)

Sub-line	Developed by	Generations untreated	Resistance to		Ref.
			Amethopterin	Dichloroamethopterin	
M46R	Amethopterin treatment of *L*1210	81	complete	moderate	11, 12
M66-3R	Dichloroamethopterin treatment of *L*1210	17	marked	marked	12, 13
C82A	Dichloroamethopterin treatment of *M46R*	8	complete	complete	13
8-Azaguanine resistant	8-Azaguanine treatment of *L*1210	58	none	none	14

antifolate-sensitive and antifolate-resistant sub-lines of mouse lymphoid leukæmia *L*1210. Marked increases of enzyme activity have been found in resistant cells grown for many generations in the absence of the antifolates. The implications of high enzyme-levels are discussed not only in relation to the emergence of resistant cells but also to possible utilization of this activity to achieve lethal synthesis with new kinds of folic acid antagonists.

During investigations on the influence of chemotherapeutic agents against systemic lymphoid leukæmia (*L*1210) in mice, various antifolate-resistant sublines were developed. A summary of information on these sublines is given in Table 1. In addition to the antifolate-resistant sub-lines, an 8-azaguanine variant of leukæmia *L*1210 was also studied. It had been produced by treatment with 8-azaguanine over a number of generations[14]. This variant is cross-resistant to 6-mercaptopurine and shows increased sensitivity to amethopterin[14].

The tissues used were obtained from normal 12-week-old *CDBA* male mice and from mice of the same cross implanted with various lines of antifolate-sensitive and antifolate-resistant lymphoid leukæmia. The tumour tissue was solid tumour which grew at the site of implantation. 8–11 days after inoculation the mice were killed, and the tissues were removed and quick-frozen in beakers submerged in solid carbon dioxide and acetone. One part of frozen tissue (usually the combined material from several animals, Table 2) was homogenized in a Waring Blendor with ten parts of acetone at −20°, collected on a paper filter, washed three times with cold acetone and finally dried at room temperature *in vacuo*. The powders were stored *in vacuo* at 2–4°. Extracts were prepared by mixing one part of acetone powder with ten parts of 0·05 *M* potassium phosphate buffer *p*H 7·5–0·01 *M* 2-mercaptoethanol for 15 min. at 0° and then centrifuging at 10,000 r.p.m. at 4° for 45 min. The supernatant fluid was used for the enzyme assays.

The enzymatic oxidation of reduced triphosphopyridine nucleotide by dihydrofolate was determined by measuring the decrease in absorbance at 340 mμ over a 5-min. period[15]. The complete incubation mixture consisted of 3·0 ml. of 0·05 *M* potassium phosphate buffer *p*H 7·5–0·01 *M* mercaptoethanol, 0·1 μmole of dihydrofolic acid (prepared by reduction of folic acid with sodium dithionite[16]), 0·2 μmole of reduced triphosphopyridine nucleotide and 50 μl. of enzyme extract. The number of millimicromoles of dihydrofolate reduced was calculated from the decrease of absorbance at $\lambda = 340$ mμ on the basis of $\Delta\varepsilon = 11{,}270$ due to the combined decrease of $\Delta\varepsilon = 6{,}220$ (reduced triphosphopyridine nucleotide oxidized to triphosphopyridine nucleotide) plus $\Delta\varepsilon = 5{,}050$ (dihydrofolate reduced to tetrahydrofolate). Protein content was determined by the method of Lowry *et al.*[17]. Each value was corrected for a minor change in absorbance which occurred in the absence of dihydrofolic acid.

The enzyme activity data are summarized in Table 3. A comparison of dihydrofolate reductase activities in the solid tumours which had grown at the site of implantation of leukæmic cells reveals the following: *M46R* (sub-line of *L*1210 which had developed resistance to amethopterin) had four times the activity of the sensitive *L*1210. *M66-3R* (sub-line of *L*1210 which had developed resistance to dichloroamethopterin) showed no increase in activity over that of the sensitive *L*1210. However, *C82A* (sub-line of *L*1210 made doubly resistant to amethopterin and dichloroamethopterin) had more than 29 times the activity of the original sensitive line. Thus when two closely related folic acid antagonists were used in sequence to develop a sub-line of leukæmia which was doubly resistant to both drugs, leukæmic cells emerged with very high levels of dihydrofolate reductase activity. Enzyme induction was probably not involved since high levels of enzyme were maintained in resistant cells grown for many generations in the absence of antifolate.

The enzyme activities of spleens of leukæmic animals were essentially the same as those obtained with the solid tumours. On invasion by leukæmic cells the spleen increased from a normal average weight of 0·1 gm. to 0·5 gm. Thus approximately 80 per cent of the spleen may have consisted of leukæmic cells. The assumption here would be that the leukæmic process had not caused in addition the entrance or proliferation of normal cells. After invasion by leukæmic cells the spleen, which normally

Table 2

Source of tissue	Average wet weight (gm.)			Animals per assay			Number of assays		
	Liver	Spleen	Tumour	Liver	Spleen	Tumour	Liver	Spleen	Tumour
Normal	1·67	0·10	—	7	6	—	7	8	—
*L*1210	2·41	0·50	0·20	6	7	7	7	6	5
M46R	2·44	0·52	0·27	6	7	8	6	5	4
M66-3R	1·84	0·58	0·26	5	5	8	4	4	3
C82A	2·50	0·50	0·30	3	3	8	5	4	4
Azaguanine resistant	2·50	0·75	0·60	3	4	4	2	2	2

Table 3. Dihydrofolate Reductase Activities

Source of tissues	mμmol. of dihydrofolate reduced per mgm. of protein per hr. at 28° (mean ± S.E.)		
	Liver	Spleen	Tumour
Normal	51 ± 6	11*	—
L1210	60 ± 8	59 ± 7	53 ± 10
M46R	113 ± 10	222 ± 26	225 ± 41
M66–3R	52 ± 4	55 ± 11	53 ± 5
C82.4	413 ± 88	1,340 ± 155	1,535 ± 105
Azaguanine resistant	61†	68†	75†

* In five assays the activity was almost zero.
† Average of two assays.

had very little if any dihydrofolate reductase, exhibited markedly increased enzyme activity of the same order as that observed for tumour.

The infiltration of the liver by leukæmic cells, although not as extensive as in the spleen, was also accompanied by an increase of dihydrofolate reductase activity. Again the pattern of activities of the various sub-lines paralleled the tumour activities. If it is assumed that the increased weight of the livers from leukæmic mice (Table 2) is caused by infiltration of leukæmic cells having the same enzyme activity as the cells of the solid tumour, then it is possible to calculate the approximate enzyme activity which can be expected in various samples of leukæmic liver. For *M46R* liver the predicted value obtained in this manner was 106 as compared with an actual value of 113 (Table 3). For *C82.4* liver the predicted and observed values were 544 and 413 respectively.

Attempts to explain the phenomenon of resistance should be tempered with the realization that knowledge of the biochemical basis of resistance gained by study of one type of cell may not be applicable to other kinds of cells. It has been suggested that the major factor in the development of resistant *S. faecalis* is the reduction in the permeability of the bacterial cell to the antifolates[18]. The occurrence of such a change in leukæmic cells has not been definitively established. Aronow has attributed the resistance of mouse fibroblast cells grown in tissue culture to possible changes in enzymes concerned with tetrahydrofolic acid utilization[19].

Table 4. Inhibitory Effects of Three Antifolates on Dihydrofolate Reductase Activities of Sensitive and Resistant Leukæmias

Source of enzyme	Uninhibited enzyme	Enzyme + aminopterin $1{\cdot}0 \times 10^{-8}$ *M*	Enzyme + amethopterin $0{\cdot}5 \times 10^{-8}$ *M*	Enzyme + dichloroamethopterin $0{\cdot}25 \times 10^{-8}$ *M*
Normal liver	38	12	18	15
L1210 spleen	38	10	11	11
Azaguanine-resistant spleen	43	11	11	12
Dichloroamethopterin-resistant spleen, *M66–3R*	37	12	12	11
Amethopterin-resistant spleen, *M46R*	106	65	58	83
Amethopterin and dichloroamethopterin-resistant spleen, *C82.4*	890	700	650	645

Twenty μl. of enzyme extract and 2·16 μl. of inhibitor in 2 per cent sodium carbonate (final concentration of antifolate is shown in the table) were pipetted into 1·0 ml. of 0·05 *M* potassium phosphate buffer, *p*H 7·5, 0·01 *M* 2-mercaptoethanol and incubated at 34° for 3 min. Then 0·07 μmole of reduced triphosphopyridine nucleotide and 0·02 μmole of dihydrofolic acid were added. All activities are expressed as decrease of absorbancy at 340 mμ in 5 min. All values are corrected for optical density changes which occur in absence of dihydrofolic acid and have been multiplied by 1,000 for greater ease of comparison. The 5-min. values for *C82.4* enzyme are based on optical density changes obtained during the first minute of incubation because the high activity leads to rapid depletion of the substrate

If the inhibition of leukæmic cell growth by amethopterin is due mainly to the inhibition of dihydrofolate reductase, the simplest explanation of resistance would be either an increase of the enzyme or a decrease in permeability to the drug or both. So long as drug-levels *in vivo* are maintained at low levels and cell permeability is not limiting, leukæmic cells with high dihydrofolate reductase activity should have a better chance to survive than cells with low dihydrofolate reductase activity. It is easy to demonstrate with cell-free extracts *in vitro*, where permeability does not play a part, how high levels of dihydrofolate reductase could help to explain resistance. For example, despite inhibition by amethopterin at a concentration of $0{\cdot}5 \times 10^{-8}$ *M*, there was more dihydrofolate reductase activity left in the inhibited enzyme preparation from resistant leukæmic cells than in the uninhibited extracts of sensitive *L1210* cells (Table 4). This difference cannot be attributed to a change in affinity of drug with enzyme since preliminary kinetic studies with enzyme extracts from sensitive *L1210* and resistant *C82.4* spleens indicate that the K_I values with amethopterin for both enzymes are approximately the same, 5×10^{-11} *M*. Recently, Hakala *et al.*[20] and Fischer[21] have reported that amethopterin-resistant cells grown in tissue culture have markedly increased levels of folic acid reductase with no change in drug-enzyme affinity.

If the main site of amethopterin-binding in tissue is the enzyme it inhibits[20–24], and drug ingress is not limiting, then a high extracellular concentration of the drug (relative to the very low dissociation constant of enzyme-inhibitor complex) should result in cells with completely inhibited enzyme. One would expect on this basis alone that leukæmic cells with high enzyme-levels such as in *C82.4* would sweep up the drug to a point of complete inhibition. In this situation cells with a genetic capacity to produce more enzyme would not necessarily be favoured during a period of selection of drug-resistant cells. Amethopterin at a daily optimal dose-level of 1·0 mgm. per kgm. effectively prolongs the life-span of mice with advanced leukæmia[25]. This dose is equivalent to a calculated peak-level (assuming uniform distribution) in the tissues of 2×10^{-6} *M*, a concentration which should be more than enough to inhibit completely dihydrofolate reductase activity in extracts.

The data in Table 5 show that within 4 hr. after injection of various antifolates into leukæmic mice, the dihydrofolate reductase-levels of the doubly resistant sub-line *C82.4* tissue were much above the enzyme activity of sensitive cells. During this period the drugs had obviously been absorbed from the site

Table 5. *In vivo* Effects of Three Antifolates on Dihydrofolate Reductase Activities of Sensitive and Resistant Leukæmias

Source of tissues	mμmol. of dihydrofolate reduced per mgm. of protein per hr. at 28°			
	No drug*	Amino-pterin 0·1 mgm./kgm.	Amethopterin 1·0 mgm./kgm.	Dichloro-amethopterin 100 mgm./kgm.
Azaguanine-resistant, antifolate-sensitive leukæmia				
Liver	61	1·2	1·1	0
Spleen	68	1·0	0·5	1·8
Tumour	75	1·4	0·4	0
Antifolate-resistant leukæmia, C82.4				
Liver	413	301	259	36
Spleen	1,340	723	862	121
Tumour	1,535	1,720	1,460	580

* Data from Table 3 for comparison.
Antifolates were dissolved in 2 per cent sodium bicarbonate and administered subcutaneously in the axillary region. Four hr. later the mice were killed, tissues removed and assayed as described elsewhere in this article.

of subcutaneous injection, since in a control experiment the enzyme activity was almost abolished in tissues of mice implanted with the antifolate-sensitive azaguanine-resistant variant of *L*1210.

It is concluded that although increased dihydrofolate reductase activity may be an important factor in the development of resistance in the mouse leukæmia sub-lines, equally as important may be a limitation on the entry of the antifolates into the leukæmic cell. That increased dihydrofolate reductase activity cannot be the sole basis of resistance is apparent from our work with the sub-line *M*66-3*R* which had become resistant to dichloroamethopterin without a change of enzyme-level (Table 3). This, however, may be a unique situation associated with certain puzzling properties of the interesting dichloro-derivative.

Experiments with mice show that the optimal therapeutic dose of dichloroamethopterin is approximately 100 times that of amethopterin[26]; yet on the basis of our enzyme work, dichloroamethopterin is approximately 3–4 times as potent a dihydrofolate reductase inhibitor as aminopterin (Table 4). This may be due to a permeability barrier in the leukæmic cell wall to dichloroamethopterin. It is also of interest to point out that cells that had become resistant to amethopterin still showed some sensitivity to dichloroamethopterin. Another example of the uniqueness of dichloroamethopterin is that it produced apparent 'cures' in the mouse leukæmia system whereas aminopterin and amethopterin merely prolong the life-span of leukæmic mice[26]. 'Cured' mice develop an immunity to re-inoculation with fresh leukæmic material[19]. Dichloroamethopterin, despite its similarities to amethopterin, that is, inhibition of dihydrofolate reductase and reversal of its actions in animals with citrovorum factor[26], may owe its therapeutic efficacy to some other locus of action, perhaps the blocking of folic acid entry into cells.

If the resistance in human leukæmia can be shown to be comparable to that found in our work on mouse leukæmia, that is, a marked increase of dihydrofolate reductase occurring in leukæmic cells that have developed resistance to antifolates, then analogues of folic acid which act quite differently from aminopterin or amethopterin should be synthesized. The analogue should have the following properties: rather than inhibiting dihydrofolate reductase, it would act as a substrate for the enzyme. In its oxidized form it should be non-toxic and need not be effective against leukæmic cells that are sensitive to the action of amethopterin. The new agent after reduction should then be capable of inhibiting various reactions involving tetrahydrofolic acid. For example, one might seek for a tetrahydrofolate analogue which inhibits the biosynthesis of thymidylic acid, methionine or purines. According to this reasoning, those cells which have become resistant due to an increased dihydrofolate reductase activity could produce more lethal synthesis of a reduced pteridine which could then have the unique property of inhibiting various tetrahydrofolate-requiring metabolic reactions. The new antifolate would not be used until resistance developed and only in situations where the resistance was due to higher levels of dihydrofolate reductase in leukæmic cells. There are at least two examples where resistance appears to be due to the inability of a cell to carry out lethal synthesis, namely, the conversion of 6-mercaptopurine (or 8-azaguanine)[27] and the conversion of 5-fluorouracil[28] to the corresponding nucleotides. The situation envisaged in this article is quite the opposite; resistance would lead to lethal synthesis if the proper antifolate were used only after resistance had occurred.

This investigation was supported in part by a research grant (*Cy*-4167) from the United States Public Health Service.

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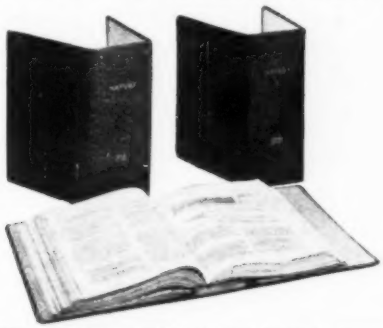

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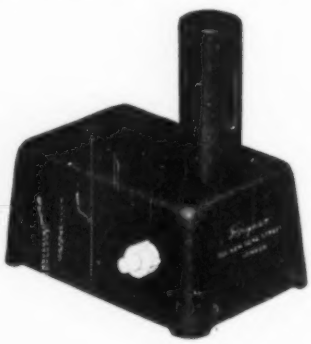

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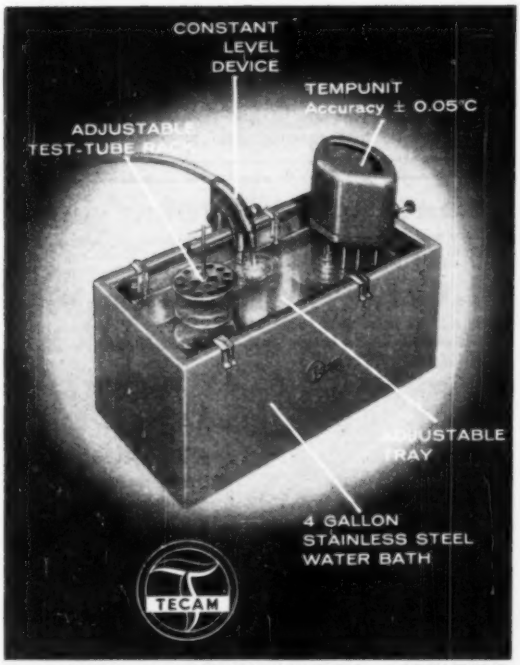

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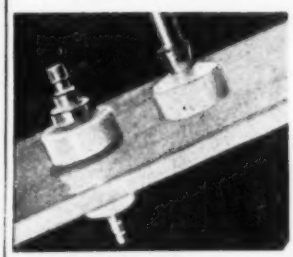

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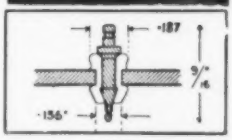

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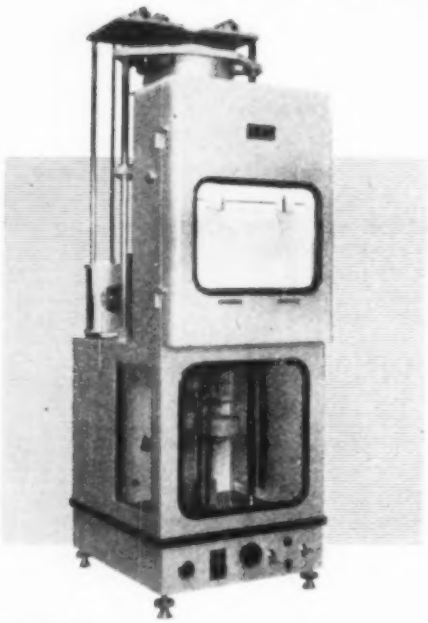

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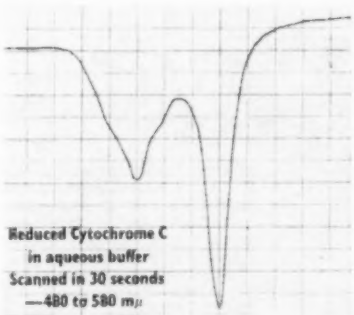

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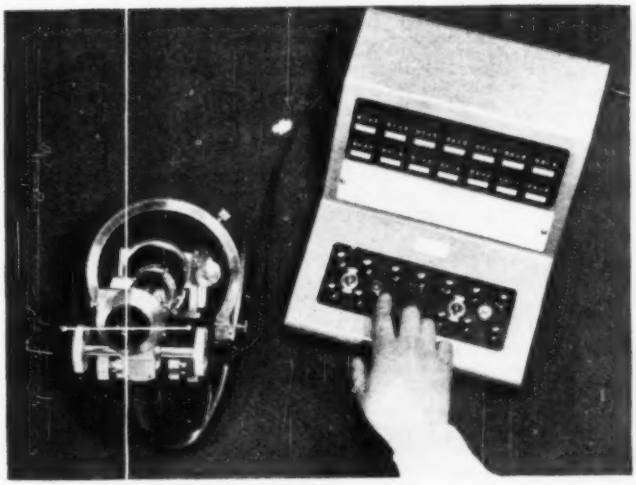

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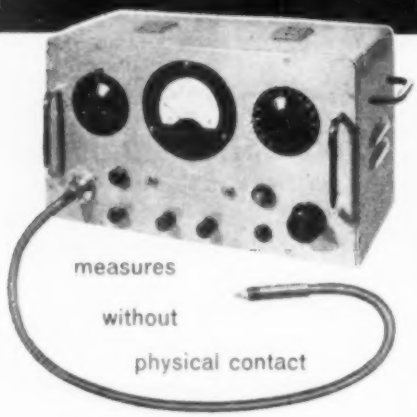

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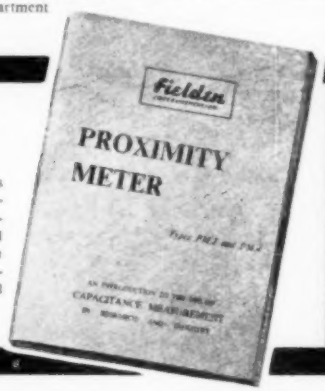

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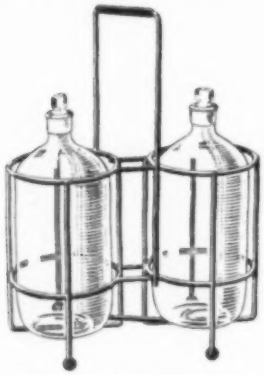

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LETTERS TO THE EDITORS

SPACE SCIENCE

Existence of Net Electric Charges on Stars

V. A. Bailey[1] has urged that a variety of geophysical and astrophysical phenomena can be explained by a net charge on the Sun of $-1{\cdot}5 \times 10^{29}$ e.s.u., admitting that this proposal is at variance with some of the "most cherished notions"[2] of theoretical astrophysicists. Attention may therefore be directed to certain deductions from Bailey's hypothesis that are in conflict with unambiguous evidence from observation as well as with what is generally regarded as sound theory.

(1) Bailey suggests two explanations of how the solar charge can be produced and maintained. The first derives from the assumption that neutrinos carry a positive charge in the range between 10^{-15} and 10^{-19} times the electron charge. Now, since the conductivity of the solar material is of the order of 10^{12}–10^{17} e.s.u. (ref. 3), the field created by the leaking of positive charges from the solar core would tend to push electrons off the solar surface at such a rate that there would be no net charge left on the Sun. Accordingly, electrons would have to drift outward, and whether a sufficiently high rate of escape materializes, or fails to, depends on the drift velocity required to compensate the postulated rate of charge production entailed by the nuclear reactions. From Bailey's figures we conclude that less than 1 electron per cm.^{2} and sec. must leave the solar surface. This rate of escape corresponds to a mean drift velocity of free electrons, in the photosphere, for example, of much less than 1 cm./sec., which is a negligible fraction of the average thermal velocity. By the same argument, it follows that this outward current would not stop in the solar corona, or even in interplanetary space. We do not carry this argument forward beyond the confines of the planetary system, since there cannot result a net charge within, say, the Earth's orbit.

(2) Having concluded that the charge production must be so fast that it cannot be compensated by currents, one might fall back on Bailey's alternative explanation and postulate the existence of a polydimensional space, such that charge conservation need not hold exactly in our four-dimensional world. The steady-state charge would be determined essentially by the local value of the conductivity and might follow closely the mass distribution. Then, of course, the atoms of the photosphere are moving in an electric field corresponding to a point charge of $-1{\cdot}5 \times 10^{29}$ e.s.u. at the centre of the Sun. This field ought to produce an excessive Stark effect. A simple calculation with well-known formulæ[4] shows that, for example, the numerous Stark components of the H_β-line would spread over 1000 Å., or so. The observed line width is of the order of 1 Å. In particular, and this is the crucial point, in the case of H_β no undisplaced component should be found at 4861 Å. This implication of Bailey's hypothesis is simply not borne out by the solar observations. By the same argument one can rule out electric fields in the chromosphere (flash spectrum) and the corona (ultraviolet emission lines). Hence, Bailey's second mechanism is incompatible with all spectroscopic evidence.

(3) Bailey's hypothesis predicts the wrong polarity for the general magnetic field of the Sun at the present epoch. Even if one agrees with Bailey in regarding the recent reversal of the solar field as the outcome of some intervening process, one may well question the appropriateness of calling this reversal a "secondary effect"[2], inasmuch as the primary effect was predicted with the wrong sign. Neither is it helpful to appeal, in support of his hypothesis, to the fact that for five stars the ratio of magnetic moment to angular momentum was supposed to be constant. It is well known that the early data on magnetic stars referred to are superseded[5]. Rather it has become obvious that the main feature of stellar magnetism is its enormous variability, and there is now little point in appealing to a mechanism which can produce only a constant field.

(4) Bailey's model could be subjected to test by terrestrial experiments. The ionosphere, according to Bailey, shields the Earth from the solar electric field, but not from its magnetic effects. Consequently, if magnetically polarizable particles are accelerated, to nearly the velocity of light, in a direction perpendicular to the radius vector Sun-Earth, in the reference frame of such particles there would exist a magnetic field of about 100 gauss, and it should be possible to measure the resulting polarization. Also, observers travelling by jet planes past the same point in opposite directions, perpendicular to the radius vector Sun-Earth, would record values for the local field differing by 20%, provided that the direction of flight was so chosen as to make the excess field parallel to the local terrestrial field.

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Kenelm W. Philip

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[1] Bailey, V. A., *Nature*, **188**, 508 (1960).
[2] Bailey, V. A., *J. Atmos. Terr. Phys.*, **18**, 256 (1960).
[3] Oster, L., *Z. Astrophysik*, **42**, 228 (1957).
[4] Unsöld, A., "Physik der Sternatmosphären", second ed., 320 (Springer Verlag, Heidelberg, 1955).
[5] Babcock, H. W., *Astrophys. J.*, **128**, 228 (1958); *ibid.*, Supp., **3**, 141 (1958).

The following comments may be made on the communication by Oster and Philip concerning my article in *Nature*[1] and note in the *Journal of Atmospheric and Terrestrial Physics*[2].

Their introductory paragraph states: "Attention may therefore be directed to certain deductions from Bailey's hypothesis that are in conflict with unambiguous evidence from observation as well as with what is generally regarded as sound theory".

This claim cannot relate to their sections 1 and 2, for these refer only to two subsidiary hypotheses on the origin of the solar charge rather than to the main hypothesis, namely, its existence. At most, the arguments in these sections can lead only to the conclusion that the corresponding hypotheses of origin, H_1 and H_2, are untenable and that the origin of the

solar charge remains to be discovered. Thus, so far as these two sections are concerned, the main hypothesis, that the Sun carries a large negative charge, remains intact.

Also, the argument in their section 2 which rules out the existence of strong electric fields below the coronal regions in which ultra-violet lines occur could serve as well to locate the solar charge mainly above these regions as to exclude the hypothesis H_2. This location is consistent with the conclusions given in the addendum to a paper published elsewhere[2].

The assertion made in their section 3, that "Bailey's hypothesis predicts the wrong polarity for the general magnetic field of the Sun at the present epoch", is itself wrong, for the Sun rotates like the Earth from west to east, and so its negative charge would impart to it a magnetic moment which is directed from north to south, with the result that the polar fields of the Sun would have the same directions as those observed by Hale and Langer, and, since 1958, by Harold D. Babcock[4]. This assertion by Oster and Philip could be right only if their phrase "at the present epoch" refers to some period later than the date of Babcock's report.

Their criticism, in section 3, of the original appeal to Blackett's comparison of the mean of five stars with the Sun does not affect the hypothesis on the solar charge; it merely throws doubt on Blackett's conclusion and so removes from consideration the last of the five different astronomical phenomena which the main hypothesis helped to explain.

The experimental tests suggested in their section 4 may be worth making provided that it is borne in mind that the medium surrounding the Earth may act as a partial magnetic screen. But, in accordance with the more recent revised estimate[3] of the solar charge as being about -3×10^{27} e.s.u., their estimate of the polarizing field should be reduced from 100 gauss to about 20 gauss or less and their estimate of the difference between the field intensities recorded by observers in oppositely travelling jet planes should be reduced from 20γ to 4γ or less.

Other experimental tests have been suggested earlier[1,3,5]. The launching, on March 11 last, of the solar artificial satellite *Pioneer* V has now (inadvertently) provided three of these tests. For the findings of the magnetometer of this satellite between March 11 and April 30 have now been published and so may be compared with the predictions, on apparent interplanetary fields, to which one is led by considering alone the hypothesis on the solar charge.

Such a comparison is made in the following communication. There it is shown that from the magnetic findings of *Pioneer* V during the first fifty days of its motion and from the simultaneous magnetic records made at Fort Belvoir (near Washington, D.C.) it is possible to arrive at the following conclusions concerning the quiet-time field vector $\mathbf{B_q}$ and the storm-time field vectors $\mathbf{B_s}$ recorded by the magnetometer in *Pioneer* V: (1) $\mathbf{B_q}$ was perpendicular to the ecliptic; (2) $\mathbf{B_q}$ was very probably directed from north to south; (3) the magnitude of $\mathbf{B_q}$ was about 2·5 gammas; (4) the storm fields $\mathbf{B_s}$ were very probably perpendicular to the ecliptic and directed from north to south, while the peak value of these fields was about 50γ.

The conclusions (1) and (2) agree exactly with the direction and sense of the magnetic field $\mathbf{H_r}$ induced by the motion of a negatively charged Sun relative to an inertial frame attached to the satellite. The conclusion (3) is within a factor of about 50 of the value 130γ for $\mathbf{H_r}$ which is yielded by the revised estimate -3×10^{27} e.s.u. for the solar charge; this suggests that *Pioneer* V may have been surrounded by a diamagnetic cloud of ionized hydrogen. The conclusion (4) promises to be significant in regard to theories of geomagnetic storms.

These conclusions and the discussion in the previous paragraph constitute evidence in favour of the solar charge hypothesis that is at least as cogent as most evidence against it, which is based on long-current views about the physical conditions in extra-terrestrial space or in the Sun. For nearly all such views are the result of combining direct observation from the Earth's surface with current extrapolations of physical theories to large and remote astronomical bodies or regions and it is well known that this practice has more than once led to erroneous conclusions.

With regard to any other astrophysical evidence which may be adduced for or against the solar charge hypothesis, it is essential to apply the present general principle of theoretical physics (which may be extended to include astrophysics and cosmology) that the sole purpose of this subject is "to calculate results that can be compared with observation" (Dirac).

V. A. Bailey

University of Sydney.
Nov. 24.

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[2] Bailey, V. A., *J. Atmos. Terr. Phys.*, **18**, 256 (1960).
[3] Bailey, V. A., *J. Proc. Roy. Soc., N.S.W.*, **94**, 77 (1960).
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Apparent Steady Component of the Interplanetary Magnetic Field

In a recent communication, P. J. Coleman, jun., C. P. Sonnett, D. L. Judge and E. J. Smith[1] gave a preliminary report on findings provided by the magnetometer carried by the space probe *Pioneer* V during the first 50 days of operation. For brevity, this publication will be referred to as ref. 1.

In a later publication, P. J. Coleman, jun., Leverett Davis and C. P. Sonnett[2] reported more specifically on "an apparent steady component of the interplanetary magnetic field". This component is also termed a "quiet time field" in ref. 1 which speaks of "The sudden increases in magnetic field strength during solar activity and the apparent existence of a quiet time field perpendicular to the ecliptic".

For convenience, we shall here denote the apparent quiet-time field vector by $\mathbf{B_q}$, the "sudden increases" or storm-time field vectors by $\mathbf{B_s}$ and the total field $\mathbf{B_q} + \mathbf{B_s}$ by $\mathbf{B}$. Also the field variation vectors observed on the Earth's surface during the main phase of a storm will be denoted by $\mathbf{F_s}$.

Although ref. 1 states that the quiet-time vector $\mathbf{B_q}$ is perpendicular to the ecliptic, neither reference states the sense of this vector. As a knowledge of this sense is essential to any theory of the origin of this quiet-time field, I shall present here arguments which appear to show that from the facts stated in refs. 1 and 2 and from the well-established facts concerning the direction and sense of terrestrial storm fields $\mathbf{F_s}$, we may infer that very probably the quiet-time field $\mathbf{B_q}$ is directed from the north to the south of the ecliptic.

These facts may be set out as follows in four groups, 1–4.

(1) The two graphs in Fig. 2 of ref. 1 which give as a function of time the average measured values of $\mathbf{B}_\perp$, the field component perpendicular to the ecliptic, and the magnetic a-indices recorded at Fort Belvoir (near Washington, D.C., and so in latitude 38° 53′ N.) during the solar event which commenced on March 31 and ended on April 3, 1960. These graphs are strikingly similar throughout and have their main peak values, 50γ and a-index 400, near the beginning of April 1.

(2) During this event *Pioneer* V was about 6 million km. distant from the Earth and both were about 150 million km. from the Sun, that is, *Pioneer* V was both well outside the influence of the Earth's magnetic field and near to the Earth within about 4 per cent of the Earth's distance from the Sun.

(3) The terrestrial storm field vectors $\mathbf{F}_s$, at medium and lower latitudes and during the main phase of a storm, are in general nearly parallel to the Earth's magnetic axis and directed from north to south, that is, $\mathbf{F}_s$ is nearly perpendicular to the ecliptic and directed from the north to the south. Also, in such latitudes the storm-time variations in the magnitude of the horizontal component of the Earth's field are in general much larger than those of the other two components (this could perhaps be verified by examination of the records at Fort Belvoir), and so the a-index is a statistically consistent measure of the magnitude F_s of the storm-field $\mathbf{F}_s$.

(4) In Fig. 2 of ref. 1 the value of the component $\mathbf{B}_\perp$ of the total field $\mathbf{B}$ was never less than the observed magnitude, 2·5γ, of the quiet-time field $\mathbf{B}_q$. Fig. 2 of ref. 2 shows that approximately the same fact was observed over the much longer period of 15 days, March 27–April 11, and during 22 other days.

On these four sets of facts we may base the following arguments:

(*a*) By (1), during the period of the solar event the Sun produced simultaneously a magnetic storm field $\mathbf{B}_s$ at *Pioneer* V and a magnetic storm field $\mathbf{F}_s$ at the Earth which vary together quite similarly in time. Since by (2) these two fields occurred in a region with radial dimensions only 4 per cent of its distance from the solar source of these fields it is very probable that they were parallel to one another. It is also probable that they both arose from an apparent parallel field $\mathbf{H}_s$ produced by the Sun throughout this region.

(*b*) By (3) and (*a*) it now follows that very probably $\mathbf{B}_s$ was nearly perpendicular to the ecliptic and directed from the north to the south.

(*c*) Since $\mathbf{B}_q$ was also perpendicular to the ecliptic it follows from (*b*) that $\mathbf{B}_q$ was very probably nearly parallel to $\mathbf{B}_s$. Hence the total field $\mathbf{B} = \mathbf{B}_q + \mathbf{B}_s$ was probably nearly perpendicular to the ecliptic, and so its magnitude would be given by the observed field $\mathbf{B}_\perp$ perpendicular to the axis of spin of *Pioneer* V, for this axis is nearly parallel to the ecliptic.

(*d*) If the sense of $\mathbf{B}_q$ had been opposite to that of $\mathbf{B}_s$ the magnitude of $\mathbf{B}$ and therefore also $\mathbf{B}_\perp$ would often have become much less than 2·5γ. Since this never occurred during the 37 days mentioned under (4), it follows that $\mathbf{B}_q$ always had the same sense as $\mathbf{B}_s$.

(*e*) It follows from (*d*) and (*b*) that very probably the sense of $\mathbf{B}_q$ was from north to south.

We can now summarize, as follows, the interplanetary findings of the magnetometer on *Pioneer* V: (1) The quiet-time field vector $\mathbf{B}_q$ was perpendicular to the ecliptic; (2) $\mathbf{B}_q$ was very probably directed from north to south; (3) the magnitude of $\mathbf{B}_q$ was about 2·5γ; (4) the storm fields $\mathbf{B}_s$ produced by the Sun were very probably perpendicular to the ecliptic and directed from north to south. The peak value of $\mathbf{B}_s$ was about 50γ.

In their discussion of the findings labelled (1) and (3) above, Coleman *et al.*[2] refer to the "serious discrepancies between the implications of these observations and present models of the interplanetary field". It is therefore interesting to note that the findings (1) and (2) agree exactly with the direction and sense of the magnetic field vector $\mathbf{H}_r$ set up near the Earth as a result of its orbital motion about a negatively charged Sun. It should also be noted that this theoretical field $\mathbf{H}_r$ was deduced from a general hypothesis, about the charges on stars similar to the Sun, which was considered in three papers[3–5] submitted for publication before the launching of *Pioneer* V.

For a comparison of the finding (3) above with theoretical estimates of the magnitude of $\mathbf{H}_r$ reference may be made to the addendum in the third publication[5], where it is shown that the observed quiet-time field is about 55 times smaller than the nearest estimate made without considering the possible diamagnetic effects of any plasmoid in which *Pioneer* V could have been immersed[6].

It is also interesting to note that the largest observed storm field vector $\mathbf{B}_s$ appears to agree in direction, sense and order of magnitude with the theoretical vector $\mathbf{H}_r$, as calculated in the same addendum.

Despite this encouraging partial confirmation of the solar charge hypothesis it is evidently necessary to test it thoroughly by means of magnetometers and electrometers carried in space probes moving in a number of different orbits and using the appropriate Lorentz transformations as well as any theory of electromagneto-ionic media which can be developed for this purpose.

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GEOPHYSICS

Palæomagnetic Evidence Relevant to a Change in the Earth's Radius

Interest in the hypothesis that the Earth's radius has increased during geological history has been renewed in recent years because of several sets of independent observations and interpretations. From studies of the deformation of mountain ranges and the distribution of faults and oceans, Carey[1] proposes an increase in the Earth's area of 45 per cent since the Palæozoic era. Heezen[2] similarly interprets submarine topography as indicating that the oceans may be immense rift valleys formed by a pulling apart of the continents as the Earth expanded. Using a different approach, Egyed[3,4] infers a rate of increase of the Earth's radius of 0·4–0·8 mm. per

year. This calculation is based on a decrease in the total amount of continental area covered by oceans during the past 400 million years, as determined palæographically. Egyed[4] has also pointed out the desirability of using palæomagnetic data to test this hypothesis.

During the Permian period, the Earth's magnetic field was remarkably steady. Palæomagnetic studies of western European rocks of this age have a high measure of internal consistency, and these western European data, together with the results from a recent palæomagnetic study by Gusev[5] of 1,600 igneous rock samples from Siberia, now make it possible to set some limits for changes in the Earth's radius during the past 235 million years.

In an expansion of the Earth as envisaged by Carey[1], Heezen[2] and Egyed[4], the continents do not increase in area; hence, the distance between any two points on a stable part of one continent remains constant, and as the Earth's radius increases the geocentric angle between the two points decreases. If the configuration of the ancient geomagnetic field is known, then this hypothesis can be tested with palæomagnetic results. In the present analysis a dipole configuration is used: this assumption is reasonable since palæomagnetic studies have firmly established that during the past million years, at least, the geomagnetic field was very closely dipolar when averaged over 10^4 years[6]. No assumption about coincidence of the ancient magnetic and rotation axes is required.

The method used for finding the ancient Earth radius from palæomagnetic data is essentially the one originally used by Eratosthenes in the third century B.C. to obtain the present Earth radius from astronomical data. If contemporaneous palæomagnetic data from two localities on the same stable continental block have different inclinations I_1 and I_2, so that the two localities are on different circles of geomagnetic latitude, and if the ancient geomagnetic field was dipolar, then the ancient Earth radius R may be found from:

$$R = d/[\cot^{-1}(\tfrac{1}{2}\tan I_1) - \cot^{-1}(\tfrac{1}{2}\tan I_2)] \ ,$$

where d is the distance measured along the Earth's surface between the two geomagnetic latitude circles[4].

In order to evaluate the Earth's radius during the Permian period, data were analysed from palæomagnetic studies of 16 igneous and sedimentary formations from western Europe and 5 igneous formations from Siberia. Representative sampling areas in western Europe and Siberia are shown in Fig. 1, together with the virtual geomagnetic poles (fictive geocentric dipoles that would give rise to the palæomagnetically measured field direction at each locality) corresponding to the 21 data used in the present analysis. Also shown are other poles based on western European data which could not be used in the present analysis because inclination values were not published. The data analysed include the study by Creer[7] of the Exeter traps, by DuBois[8] on the Mauchline sediments and lavas; the various studies of the Esterel volcanic rocks by Roche[9], Rutten *et al.*[10], and As and Zijderveld[11]; the study by Rutten *et al.*[10] of the trachyandesites of the Oslo graben; that of Armstrong[12] of the Ayrshire kylites; the studies by Nairn[13,14] of the Niedeck porphyry, Montcenis sediments, Saint-Wendel sediments, and Rothiegendes sediments and lavas; and the study by Gusev[5] on five igneous formations from Siberia. Although the geological age of the Siberian formations

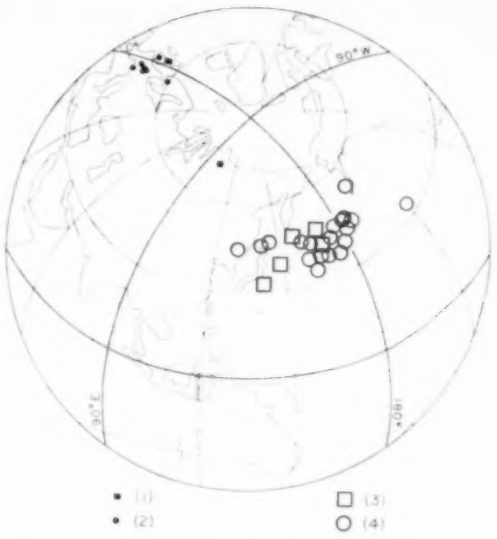

Fig. 1. Virtual geomagnetic poles calculated from western European (4) and Siberian (3) palæomagnetic data, and representative sampling localities in western Europe (2) and Siberia (1)

is subject to some uncertainty, Gusev[5] concludes that their radiometrically determined age of 250 million years is probably correct. This would correspond to mid-Permian on the new Kulp[15] geological time-scale, which incorporates recent Russian radiometric dating results.

The method of calculation is by pairing each of the 16 inclinations from western Europe with each of the 5 inclinations from Siberia for a total of 80 determinations of R. To evaluate d for each pair of inclinations, small circles were constructed passing through each sampling locality about the average Permian virtual geomagnetic pole position as the common centre; d is the linear distance on the surface of the sphere between appropriate circles. The average Permian pole position was found by statistically analysing the 21 virtual geomagnetic poles, using Fisher's[16] method.

The average of the 80 values thus calculated for the Earth's radius during the Permian is:

$$R_{\text{Permian}} = 6{,}310 \text{ km.}$$

The standard deviation of individual determinations is 1,080 km. and the standard deviation of the mean (21 independent data) is 230 km. This result is subject to an additional uncertainty if, as is quite possible, the average magnetic pole position moved during the Permian and if the time-intervals spanned by the western European data and those from Siberia are not precisely the same.

Comparing these results with the present Earth radius of 6,370 km., we come to the following conclusions. The average Permian magnetic field, as seen from two sampling areas almost 5,000 km. apart on the Eurasian land-mass, shows no significant departure from the dipolar configuration and is perfectly consistent with a Permian Earth radius equal to the present one. An increase in the Earth's radius as slow as that suggested by Egyed (0·4–0·8 mm. per year or 94–188 km. in the past 235 million years) is neither confirmed nor rejected by the palæo-

magnetic data now available. Although precise statistical confidence limits cannot be assigned to the mean value of 6,310 km. for the Permian Earth radius, an increase since the Permian as large as the 1,100 km. required to produce a 45 per cent increase in area, as suggested by Carey, appears unlikely.

Publication of this communication is authorized by the Director of the U.S. Geological Survey.

ALLAN COX
RICHARD R. DOELL

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Menlo Park, California.

[1] Carey, S. W., "Continental Drift", Symp. Univ. Tasmania, 177 (1958).
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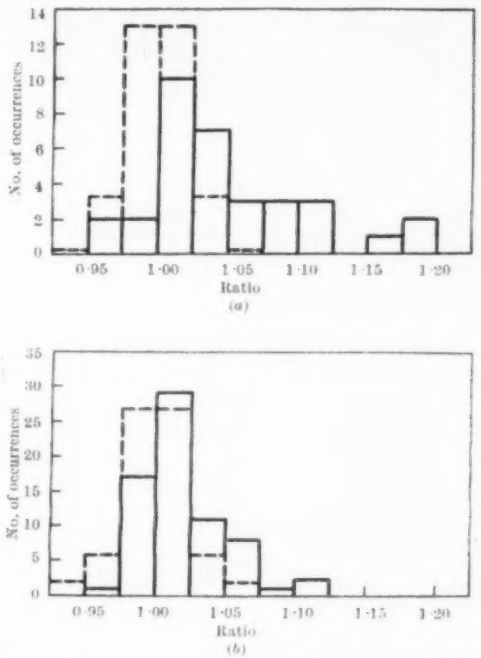

Fig. 1. Distribution of variations in *foE* about its normal value. Full line, up to 2 hr. after a solar flare; dotted line, no flare. (*a*) Class 3 flares; (*b*) Class 2 + flares

RADIOPHYSICS

Enhancement of Ionization in the *E*-Layer due to Solar Flares during the International Geophysical Year

INCREASES in the ionization of the *E*-layer have been reported after the occurrence of individual major solar flares[1,2], and an analysis by Bibl[3], for a three-month period in 1950, has shown that all increases in the critical frequency of the *E*-layer of more than about 0·2 Mc./s. above the monthly median value can be attributed to the effects of solar flares. Bibl considered only the deviations of the critical frequency from its monthly median value, and a similar analysis for 8 flares in the period 1951–56 has also been made by Taubenheim[4]. No detailed comparison has so far been made between the critical frequency after a flare and its value before the flare. Recently, in the course of other work, Minnis and Bazzard[5] have examined the hour-to-hour changes in the values of the *E*-layer critical frequency (*foE*) at Slough for the period of the International Geophysical Year. These data have been used to study the changes in *foE* associated with the occurrence of all the flares of importance 2+ and 3 which were listed in the CRPL *F*-Series Bulletins (Part *B*) and which occurred during the period 0800–1500h. U.T.

The value of *foE* for the observation at the hour immediately preceding the commencement of each flare and that for the two succeeding hours were examined in relation to the normal values for these hours. The normal value for each hour of any day was assumed to be that given by the best-fit line drawn through the points on a log *foE*–log cos χ plot for the period 0900–1500h. L.M.T. on the same day. The ratio of the observed to the normal value of *foE* was calculated for each of the three hours mentioned above. For each flare, the ratios for the two post-flare hours were then normalized by dividing by the corresponding pre-flare ratio.

The distribution of the normalized post-flare ratios for Class 3 flares is shown in Fig. 1*a*. Twenty flares have been considered which gave 33 post-flare observations of *foE*. Some post-flare observations are not available, mainly owing to the high ionospheric absorption immediately following these flares. Minnis and Bazzard[5] have shown that the standard deviation of the hourly values of *foE* about the best-fit line was approximately 2 per cent at Slough during the International Geophysical Year. The expected distribution of ratios when there are no flares can thus be calculated and is also shown in Fig. 1*a*. Application of the χ^2-test to the distributions shows that the observed increase in the frequency of occurrence of high ratios during the two hours after a flare is significant. A similar result was obtained from an analysis of 41 Class 2+ flares which gave 69 post-flare observations of *foE*. The corresponding distributions are shown in Fig. 1*b*.

The distributions for the two classes of flare are also significantly different from one another. For Class 3 and Class 2+ flares, the mean values of the critical frequency ratios are 1·05 and 1·02 respectively, while the corresponding mean times of the observations are 65 min. and 59 min. after the commencement of the flare. It should be mentioned here that, owing to the extremely high absorption which often persists for a short time after the commencement of a flare, the number of missed observations of *foE* is greater during the earlier part than the later part of the post-flare period. For this

reason, the mean ratios quoted above are probably less than they would have been if all the possible observations had been available, particularly for the more important flares.

An attempt was also made to estimate the rate at which the critical frequency returns to normal after a flare. It was not possible to measure this rate accurately as a function of time after the commencement of the flare. However, the mean rate of change of the critical frequency was found to be 3·4 per cent per hour for Class 3 flares and 1·4 per cent per hour for Class 2+ flares during the interval from approximately 25 to 120 min. after the start of the flare; this interval includes about 90 per cent of the observations of critical frequency. These observed rates of change of *foE* correspond to rates of change of electron density which are of the order of a thirtieth of those which would be expected if the layer were recovering normally from a sudden increase of ionization of the magnitude caused by the flares. It is assumed, therefore, that the observed rates of change of *foE* must represent the rate of change of intensity of the ionizing flare radiation incident on the *E*-layer. This conclusion is consistent with Taubenheim's results[4], which were, however, based on a smaller number of observations.

It is concluded from the foregoing analysis that, during the interval from about 25 min. to 120 min. after the commencement of a flare, there is a mean increase in the intensity of *E*-layer ionizing radiation which is at least 22 per cent for Class 3 flares and 8 per cent for Class 2+ flares. The mean rate of decrease of the intensity of ionizing radiation is approximately 15 per cent per hr. for Class 3 flares, and 6 per cent per hr. for Class 2+ flares.

The work described in this communication was carried out as part of the programme of the Radio Research Board and is published by permission of the Director of Radio Research of the Department of Scientific and Industrial Research.

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Skip-Distance Ray-focusing in the Ionosphere

During the period March 1–April 6, 1960, the satellite *Sputnik* 3 passed over Britain at heights below 300 km., and on some sixty occasions the 20 Mc./s. signals were received at the Radio Research Station, Slough, when the satellite was close to or beyond the horizon, propagation being by 1/2-hop and 3/2-hop modes as has been reported for earlier satellites[1]. In the 1/2-hop mode the signal is reflected directly from the ionosphere to the receiving point, and, for the 3/2-hop mode, one ground reflexion precedes the ionospheric reflexion. Under these conditions, evidence has been obtained of strong focusing by the ionosphere of waves travelling along paths close to the skip-distance path.

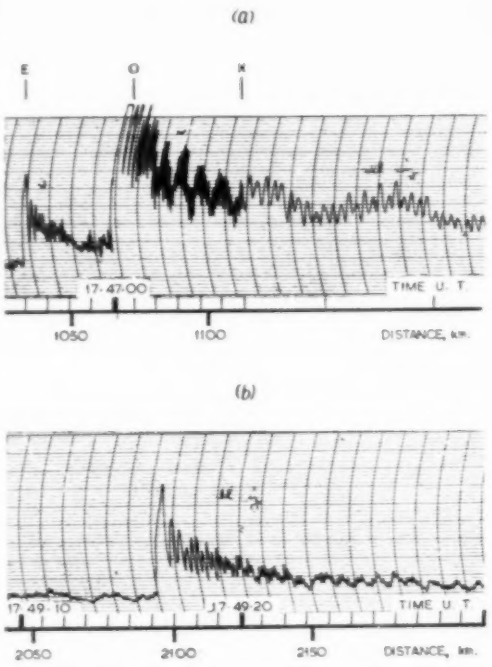

Fig. 1. Examples of skip-distance ray focusing 20 Mc./s. *Sputnik* 3 continuous wave transmissions, March 1, 1960.
(*a*) 1/2 Hop; (*b*) 3/2 hop

For example, on near overhead transits, it was noticed that as the signal from the receding satellite began to fade out, a sudden burst of signal-strength occurred, which was often as strong as, and sometimes stronger than, the signal at nearest approach, and was followed by an oscillatory decay as illustrated in Fig. 1. The pitch of the audio-frequency note heard on the receiver due to the beating of the signal with a fixed reference frequency had a warbling characteristic during this period.

Fig. 1*a* shows an amplitude record of one such occurrence. Time marks at 1-sec. intervals are shown, together with the distance to the sub-satellite point. At point *X* the recording paper speed was increased five times. During this transit the satellite passed from north-west to south-east at 200 km. altitude, and the aerial used was a horizontal dipole oriented in a north-west–south-east line. The bursts of signal are attributed to the satellite crossing the 1/2-hop skip-distance boundaries: the first burst (*E*) occurring at the crossing of the boundary for the extraordinary wave, and the second, (*O*), 4 sec. later, at the crossing of the boundary for the ordinary wave. The higher-frequency oscillations (of the order of 10 c./s.) after the main burst are due to interference between the high-angle and low-angle rays, which may be received from a point beyond the skip distance; the depth of these oscillations decreases since the strength of the upper ray diminishes much more rapidly than that of the lower ray.

Appleton and Beynon[2] observed a similar phenomenon in 1946 when receiving fixed-frequency transmissions at Slough from a transmitter in Oslo. In this case events analogous to those described above were produced by the increase of skip distance

due to a decrease of F-layer ionization. The theory of skip-distance ray focusing has been described by Bremmer[3], who gives a solution for the case of transmitter and receiver at ground-level, and shows a diagram somewhat similar to Fig. 1*a*. Using approximate ionospheric data obtained at the time of transit, a parabolic model, and the solution of Bremmer, a frequency of 10 c./s. has been calculated for the frequency of oscillation just after the main peak, increasing thereafter, for a transmitter moving away at ground-level with the satellite speed of 7·9 km./sec. The observed frequency is about 4 c./s., rising to 15 c./s. after 10 sec., which is in reasonable agreement with the calculated value. In addition, the record shows an oscillation of about 1 c./s., which is believed to be due to interference between the ordinary and extraordinary wave components.

Signals of the type shown in Fig. 1*a* have been obtained on the majority of close transits, except during the severe ionospheric storm of April 1–3, 1960. On many of the close transits, clear 3/2-hop skip-distance focusing has also been obtained. Fig. 1*b* shows the 3/2-hop peak which followed the 1/2-hop peaks shown in Fig. 1*a*; although two 3/2-hop peaks are usually present, only a single peak was observed on this occasion. In one case a clear 5/2-hop peak was also observed.

These observations provide confirmation of wave interference and focusing phenomena near the boundary of the skip zone, and are in general agreement with a related theoretical analysis of Bremmer.

This work forms part of the programme of the Radio Research Board and is published by permission of the Director of Radio Research of the Department of Scientific and Industrial Research.

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PHYSICS

Standardization of Strong Electromagnetic Fields

The possible harmful biological effects of high-intensity electromagnetic radiation have become of practical importance in recent years with the development of high-power radar and communication transmitters[1]. As a result, several instruments have been designed to measure total flux density in the frequency band 30 Mc./s.–30 Gc./s. (wave-lengths, 10 m.–1 cm.). In general, these devices indicate relative values only, and suitable techniques are therefore required by means of which they can be calibrated. Some comments on this problem are given in this communication.

In principle, standard flux densities of the specified value (1–20 mW./sq.cm.) can be established by radiating a known power from a transmitter under conditions which permit the calculation of the field strength or flux density at the receiver. This method is a convenient one, for example, at frequencies of the order of 10 Gc./s. with a horn-type aerial at the transmitter. If the horn has a gain of, say, 25 db. with respect to an isotropic radiator, a flux density of 10 mW./sq.cm. is produced at a distance of 3 m. (in a wave-front which is very nearly plane) using an oscillator of about 35 W. output. However, at frequencies in the range 100 Mc./s.–1 Gc./s. a similar procedure requires relatively large, directional aerials located well above ground on an open site, and transmitter powers of the order of a kilowatt or more. There is a need, therefore, for a standard laboratory technique operating at frequencies below about 3 Gc./s. and at power-levels of 10–50 W.

Some form of 'guided-wave' system presents an attractive solution to the problem. Apart from the advantages associated with the use of relatively low power-levels, such a technique would reduce possible radiation hazards to operating personnel to a minimum. Experiments have already been carried out at the Radio Research Station with these considerations in mind, and a summary of the basic principles and some preliminary results are given here.

A 'T.E.M.'-type wave is transmitted between parallel brass plates forming a large strip-line (3·5 m. long, 60 cm. wide and 10 cm. apart), terminated in an absorbing load. The input power (10–20 W.) is conveyed to the main structure by means of a 'coaxial to strip-line' transformer, followed by a taper section and a dielectric lens. The arrangement is somewhat similar to that adopted by El-Kharadly[2] for measurements on artificial dielectrics at a frequency of 3 Gc./s. A slotted section with a movable probe enables investigations to be made of the electric field distribution in both axial and transverse directions. An approximate value of the flux density in the parallel-plate section could be derived from a knowledge of the input power, but an indirect method is preferred for precision measurements. The latter technique makes use of a small probe and crystal detector calibrated by reference to a rectangular wave-guide transmitting a known power. If the total power flowing in a rectangular wave-guide propagating the dominant, H_{10}, mode is P watts, then the maximum electric field strength, E, at the centre of the broad face is given by:

$$E = (480\, P\, \pi\lambda_g/ab\lambda)^{1/2} \text{ volts/m.} \qquad (1)$$

where λ and λ_g are the free-space and guide wave-lengths respectively, and a and b are the internal dimensions of the guide in metres. If the voltage output of the probe is V for a field strength E in the rectangular wave-guide, then the same output, V, will be given by the same probe in the parallel-plate system when a flux density W is established, which is given by:

$$W = E^2/120\pi = 4P\lambda_g/ab\lambda \quad \text{W./sq.m.} \qquad (2)$$

The above procedure has been used in experiments carried out at a frequency of 1·2 Gc./s. The voltage standing-wave ratio ($E_{max.}/E_{min.}$) in the strip-line, when terminated by a hollow wedge-type load filled with powdered carbon, is 1·1 or less, and the transverse field distribution is approximately uniform. Devices calibrated in the strip-line have included crystal detectors and thermo-junctions surrounded by absorbing material. The results obtained to date suggest that an error of less than ± 1 db. can be expected at frequencies of the order of 1 Gc./s., and experiments are in progress to investigate the method at lower frequencies. In order to avoid the construction of a large rectangular wave-guide, a coaxial line terminated in a non-reflecting load could be used

to calibrate the probe detector at frequencies of the order of one or two hundred megacycles per second.

It is important that the perturbation produced in the strip-line by the device being calibrated should be small. This should not often present any serious difficulty, however, since the monitoring devices being developed will normally have a small measuring probe remote from the main indicating equipment.

The work described above was carried out as part of the programme of the Radio Research Board. This communication is published by permission of the Director of Radio Research of the Department of Scientific and Industrial Research.

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The 'Ballas' Form of Diamond

The rare 'ballas' form of natural diamond is referred to occasionally in the literature. Ballas diamonds have been described by various authors as follows: (1) "Dense, globular aggregates of small, radially disposed diamond crystals"[1]; (2) ". . . a very hard, tough, globular mass of diamond crystals radiating from a common center"[2]; (3) ". . . a rare form of natural diamond with radial symmetry composed of apparently spherically grown layers . . ."[3]; (4) "Radial stalk-like formation of diamond crystals, or irregular growths of multiple crystals"[4].

These descriptions allude to the idea that a ballas has some type of radial structure in its crystal arrangement. Recently, I examined a polished section of a ballas with the view of determining its structure, since I could not find a photograph of such a section or imagine precisely what sort of structure would fit the published descriptions. The section was made about 0·5 mm. from the centre of a 0·70-carat stone. After a polishing operation, the stone was etched in molten potassium nitrate for 1 hr. at 700° C. A photomicrograph of the polished surface at 30 × is shown in Fig. 1. Residual scratches from the sectioning step are still visible. The centre of the sphere lies about 0·5 mm. below the × marked on the photograph.

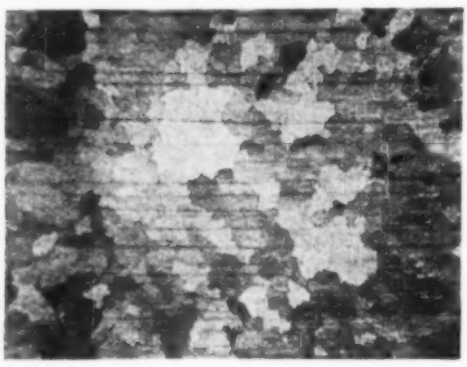

Fig. 1. Polished and etched section of a ballas diamond. (× 30)

Surprisingly, the many crystals making up the ballas do not appear to have any radial geometry. Such geometry should be revealed on a chordal plane so close to the centre of the sphere. This information indicates that previous descriptions are not precise or that the ballas at hand is an unusual variation. Part of description (4) above seems applicable to the findings. The irregularity of the crystal boundaries is an unusual feature of the structure. I should be glad to have any further information on this subject.

Williams, in his classic "Genesis of the Diamond", has shown sections of 'hailstone' bort which seems to fit description (3) above. It seems that 'hailstone' bort and ballas should not be confused as the same types.

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Frictional Oscillations

It is generally considered[1,2] that vibrations excited by friction are due to a variation of friction with velocity, μ decreasing with increasing velocity, and in some cases (unpublished work) this is so. Vibrations in sliding systems can, however, be excited by other mechanisms. Consider a rigid strut $O'P$ held in an elastic pivot O' which in turn is attached to another strut $O'O''$, the pivot O'' being stiffer than O' (Fig. 1).

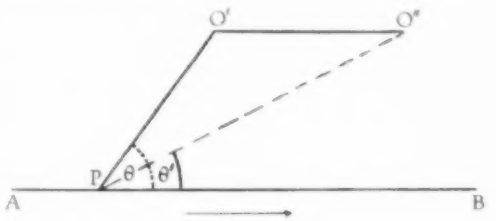

Fig. 1

The surface AB is moving past P in the direction shown and the coefficient of friction of the tip P is μ. The force F at P is given by $F = \mu L/(1 - \mu\tan\theta)$; so if $\mu = \cot\theta$, F is very large and 'spragging' occurs, that is, there is no slip between P and the moving surface AB. P is therefore displaced elastically in the direction of motion and θ increased slightly. As AB continues to move the elastic moment at the pivot O' opposing further deflexion of $O'P$ eventually becomes so large that $PO'O''$ becomes equivalent to a rigid strut $O''P$, O'' becomes the pivot point and θ is reduced to θ'. F falls accordingly so that the elastic energy stored in O' takes over and tends to swing P off the surface and slip occurs. The strut $O'P$ is therefore set vibrating and the surface AB is subjected to a periodically varying tangential force, and if AB is of suitable dimensions and elastic properties it can be set oscillating. Provided they are suitably mounted, solid bodies can be made to vibrate by a similar mechanism to the system of struts.

This sprag-slip motion can be demonstrated in several ways. If a strut OP pivoted in a rigid mount at O' is slid against a surface AB, $F=\mu L/(1-\mu\tan\theta)$ for values of $\cot\theta > \mu$; at $\cot\theta = \mu$ the strut breaks. If there are two pivot points $O'O''$, stick slip occurs at $\cot\theta = \mu$ and the oscillations of $O'P$ and $O'O''$ can be demonstrated with dial gauges or by moving smoked glass plates against probes attached to the struts. A very simple demonstration is to move a pencil held lightly at its extreme end and at its spragging angle across a sheet of paper.

The manner in which the exciter can set up vibrations in the opposing body can be demonstrated by holding a thin sheet of material edgewise against a rotating telephone bell. If the sheet is held at the spragging angle it is set in vibration and the bell emits a loud screeching sound. This sound contains a large number of harmonics, the vibrations are non-linear and their frequency is determined by the natural frequency of the vibrator as well as that of the bell. In certain circumstances elastic deflexions in the bell itself reduce the friction force; the vibrations are then confined to the bell, which emits a loud relatively pure note. The frequency of this sound is almost the same as that of the sound emitted when the bell is struck.

I wish to thank the directors of Messrs. Ferodo, Ltd., for permission to publish this communication.

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Via Stockport.

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Excitation Functions of (d,α)- and $(d,\alpha n)$-Reactions on Natural Tungsten

By irradiation in the Amsterdam cyclotron of natural tungsten with 22-MeV. deuterons, three species of radioactive tantalum were observed due to the following reactions: $^{186}W(d,\alpha)^{182}Ta$, $^{186}W(d,\alpha)^{184}Ta$ and $^{186}W(d,\alpha n)^{183}Ta$.

The chemical separation of these nuclides was performed by selective liquid–liquid extraction with di-*iso*butylketone in hydrofluoric – hydrochloric acid medium in the presence of tantalum carrier[1].

Absolute tantalum activities were determined by means of a calibrated end-window Geiger tube. The results appeared to be in excellent agreement with those obtained with a 4π proportional counter.

The maximum deuteron energy of the cyclotron was computed by fitting an experimental relative excitation function of the $^{27}Al(d,\alpha p)^{24}Na$ reaction with those obtained by Batzel *et al.*[2] and Moeken[3]. The maximum energy appeared to be 22 MeV.

The beam intensity was computed from the same reaction at the maximum deuteron energy, as absolute cross-sections for this reaction are also accurately known.

The cross-sections for the three reactions under consideration as a function of deuteron energy were computed from the measured tantalum activities, after adequate corrections for chemical yield, decay and counting efficiency of stacked tungsten foils irradiated in the internal beam of the Amsterdam synchro-cyclotron. The deuteron energy in each foil was calculated from the range–energy curve of tungsten computed from the Bethe–Livingstone equation[4]. The results are summarized in Table 1.

Table 1. Cross-sections in Millibarns as a Function of Deuteron Energy

Deuteron energy	$^{186}W(d,\alpha)^{182}Ta$	$^{186}W(d,\alpha)^{184}Ta$	$^{186}W(d,\alpha n)^{183}Ta$
21	3·05	1·25	1·15
20	2·90	1·22	0·97
19	2·65	1·08	0·67
18	2·30	0·85	0·52
17	2·10	0·70	0·35
16	1·70	0·57	0·22
15	1·30	0·46	0·13
14	1·08	0·32	0·075
13	0·90	0·21	—
12	0·62	0·13	—
11	0·29	—	—
10	0·16	—	—
9	0·05	—	—

Acknowledgments are to due Prof. A. H. W. Aten, jun., I.K.O., Amsterdam, for valuable discussions during the performance of this work.

This work is part of the research sponsored by the Institut Interuniversitaire des Sciences Nucléaires.

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GEOLOGY

Geology of the Floor of the Bristol Channel

A geological survey of the floor of the Bristol Channel was made from R.R.S. *Discovery II* between April 22 and May 2, 1960, using asdic[1–3] and bottom sampling equipment. Preliminary results are summarized in the accompanying map (Fig. 1). The northern part of the Channel is floored with superficial deposits except around Caldy Island. In the southern part there are extensive areas of exposed rock.

Upper Palæozoic rocks outcrop continuously from Hartland Point to Lundy Island. They include slates and quartzites, and the asdic records show a strong lineation orientated a few degrees north of west, which in some places appears to be bedding. The granite of Lundy Island does not extend more than a mile to the north, or half a mile to the south of the Island. We could not approach close to the east or west coasts on account of the sand banks, but believe that the outline of the Island corresponds closely to the boundary of the granite: no dykes were recognized near the Island.

Many west-north-west to north-west lineations were recorded by the asdic from the Upper Palæozoic rocks west of Ilfracombe, while eastward for 3 miles north-easterly lineations were found. At the Horse-shoe Rocks, a shoal surrounded by Upper Palæozoics about 4 miles north-west of Ilfracombe, we dredged dark green basic igneous rock comparable to a metamorphosed spilite. Skin divers have not yet established whether the spilite outcrops here, or whether it is derived from a superficial deposit.

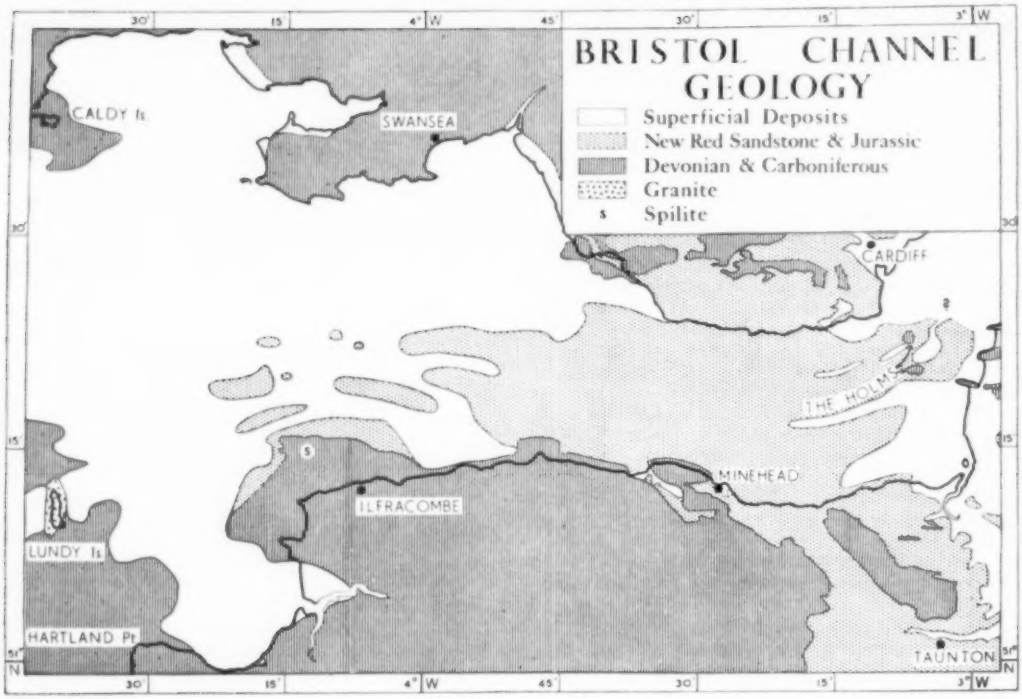

Fig. 1

From the Holms westward to beyond Ilfracombe the floor of most of the channel is composed of Liassic rocks lying nearly horizontal: these approach very close to the southern shore west of Minehead. In some places there is New Red Sandstone between the Upper Palæozoics and the Lias, but a continuous strip of New Red Sandstone is not proved.

Two asdic reconnaissance lines run between Steep Holm and Flat Holm suggest that the intervening channel is floored by Mesozoic rocks, so that these Carboniferous masses were already isolated in Mesozoic times, as supposed by Strahan and Cantrill[4].

Between Lundy Island and Pembrokeshire the superficial deposits are continuous, except for Palæozoic outcrops near the Welsh coast. Westward extension of the Mesozoics to connect with the outcrops off north Cornwall reported by Day[5] is therefore unproved, but if such a connexion exists it must lie to the north of Lundy.

Detailed analysis of the findings is in progress and will be published elsewhere at a later date.

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METALLURGY

An Unusual Feature of the Fusion Welding of Niobium to Vanadium

Theibacker, Baugh, Kasburg and Stermon[1] observed apex-shaped boundaries between the fusion zone and parent plate in zirconium–hafnium welding, but offered no satisfactory explanation.

During some recent investigations into the fusion welding of niobium to vanadium, a similar but more pronounced effect was noticed at the boundary between niobium and the fusion zone. This 'tongue effect' is illustrated in Fig. 1.

A micro-hardness traverse carried out through the tip of the tongue showed that there was no gradation in hardness as the boundary was approached on either side. The change in hardness was sudden and a

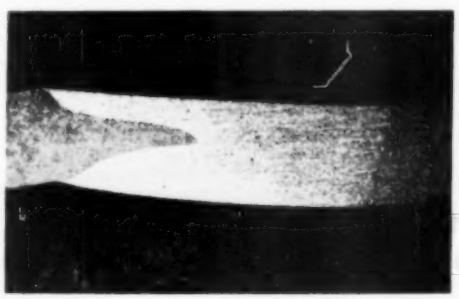

Fig. 1. Plate 1/16 in. thick

constant level persisted on both sides of the interface. The niobium parent plate had a hardness of 140 V.P.N. and the fusion zone had a hardness of 350 V.P.N. This indicated that there was virtually no diffusion layer showing a gradual fall of vanadium content in the solid niobium, but an extremely sharp division between the niobium and the fusion zone material. The same hardness conditions applied to the vanadium side of the weld.

Micro-hardness tests carried out across the tip of the tongue and parallel to the interfaces gave results in keeping with the above conditions.

The sectioning of further specimens has shown that at electrode traverse-rates of 4–5 in. per min., and given currents, or similarly at currents as low as 40 amp. and given traverse-rates, the tongue was much more blunt and under-developed. As the current increased or the traverse-rate decreased there was a definite trend from the blunt form to the sharp form of Fig. 1. In addition, it was noticed that at the start of a weld, it was necessary to melt vanadium first before the niobium became molten, at the currents used, and in fact a true bond would not form until the vanadium had run into the niobium and formed an alloy. Once this had happened welding appeared to continue normally. Thus it would seem that the temperature of the fused metal was below the melting point of niobium (2,420° C.) but above that of vanadium (1,860° C.). It was found also that in order to weld niobium to niobium, 30 per cent higher currents were required than to weld vanadium to vanadium for a similar bead width. This would be expected, when considering melting points and conductivities of the two metals.

Thus the evidence suggests that the blunt tongue is an early stage in the development of the sharper outline. This sharp contour was reached fairly quickly in the series and then was a constant feature. For example, a current of 70 amp. was used in the series of welds where traverse-rates were varied from 4 in. per min. to ½ in. per min. At a rate of 4 in. per min. the tongue was only partially formed, but at 2½ in. per min. it was complete.

It is considered that the mechanism of formation of the tongue is one of dissolution of niobium in weld metal.

A more complete treatment of this aspect will be published elsewhere.

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Effect of Air Pressure on the Fatigue of Lead and Aluminium

It is known that the fatigue strengths of lead and aluminium are affected by the presence of the atmosphere during fatigue stressing[1–4]. The present communication reports the results of experiments on the dependence of the fatigue life of lead and aluminium on air pressure at room temperature, 22° C.

Specimens were prepared from high-purity rolled strip (99·999 per cent lead, and 'super pure' aluminium), and, after annealing, were fatigued in reverse plane bending at the rate of 500 cycles/min.

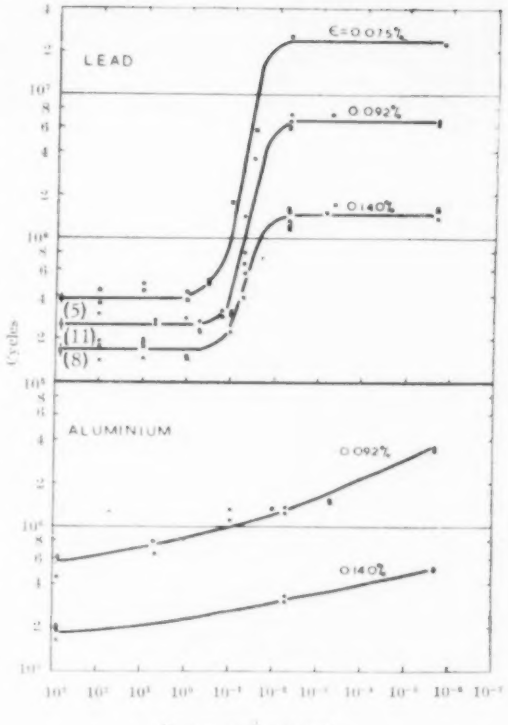

Fig. 1. Variation of log fatigue life with log air pressure. In the top figure (for lead) the figures in brackets refer to the number of specimens tested at normal atmospheric pressure; all other points are plotted

The influence of air pressure on the fatigue life at various constant strain amplitudes is shown in Fig. 1. The curves for aluminium indicate a steady increase in life with decrease of air pressure which is in agreement with the dependence on air pressure of the fatigue life of aluminium and copper found recently by Wadsworth and Hutchings[3].

In contrast, each of the three curves shown for lead displays three distinct ranges: (*a*) a high-pressure range in which the life is constant (atmospheric pressure to approx. 0·15 mm. mercury); (*b*) an intermediate range in which the life increases rapidly with decreasing pressure (approx. $0{\cdot}15–5 \times 10^{-3}$ mm. mercury); and (*c*) a low-pressure range in which the life is unaffected by further reduction of pressure (approx. $5 \times 10^{-3}–2 \times 10^{-6}$ mm. mercury). The stepped form of the curves for lead is thought to be associated with specific changes in the nature of the fatigue deformation produced by variations in the rate of reaction between the gas and the metal at different gas pressures. For example, in the high-pressure range (*a*) specimens failed by intercrystalline cracking whereas in the low-pressure range (*c*) the intercrystalline cracking was suppressed and failure occurred by extensive slip deformation[4]. On the other hand, in the case of aluminium[3], it appears that the presence of the air only affects the rate of propagation of cracks and does not affect the type of cracking. However,

it may well be that the fatigue behaviour of aluminium at elevated temperatures would show a closer resemblance to that of lead at room temperature and, conversely, that the fatigue behaviour of lead at liquid-air temperature would show a closer resemblance to that of aluminium at room temperature.

This work formed part of the research programme of Broken Hill Associated Smelters Pty. Ltd. and was carried out under the supervision of Prof. J. Neill Greenwood, to whom thanks are due for helpful discussions.

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RADIATION CHEMISTRY

Labelling of Organic Compounds by Mercury-photosensitized Reaction with Tritium Gas

The widely employed Wilzbach's tritiation method is based on the exchange reaction between an organic substance and tritium gas induced by radiation from several curies of T_2 (ref. 1).

In order to increase the exchange-rate and to reduce the amount of tritium required, several techniques have been developed which employ an external energy source for promoting the labelling process: electrical discharges[2-5], γ-rays[6], microwaves[3] have been used. Recently[7] the tritiation of two polymers by ultra-violet irradiation in the presence of tritium has been described.

We report here a simple labelling technique, based on the mercury-photosensitized exchange between tritium gas and an organic compound, which, in principle, allows the tritiation of all the substances, including those which do not absorb in the ultra-violet region. In using this method, a silica ampoule containing the organic sample and tritium gas, with a small amount of mercury, is irradiated at room temperature with a low-pressure mercury lamp. The energy of the 2537 Å. resonance line is absorbed by the mercury vapour which, as pointed out by Kaplan[8] in a detailed study on the reaction of unsaturated hydrocarbons with tritium, causes the excitation and the dissociation of both tritium and organic molecules.

Table 1

Compound	Run No.	T_2 activity (mc.)	Irradiation time* (hr.)	Specific activity in pure compound (mc./gm.)	Total activity in pure compound (mc.)
Toluene	1	10 ± 2·5	120	1·78 ± 0·01	1·53
Toluene	2	10 ± 2·5	96	0·730 ± 0·006	1·26
Toluene, blank†	—	10 ± 2·5	—	0·0053 ± 0·0002	—
*Cyclo*hexane	3	10 ± 2·5	120	0·223 ± 0·002	0·356
*Cyclo*hexane, blank†	—	10 ± 2·5	—	0·0005	—

* The irradiations were performed at 25° C., tritium gas employed having been diluted with pure hydrogen.

† In the blank runs the tritium gas and the hydrocarbons were in contact for a period of 120 hr. without ultra-violet irradiation.

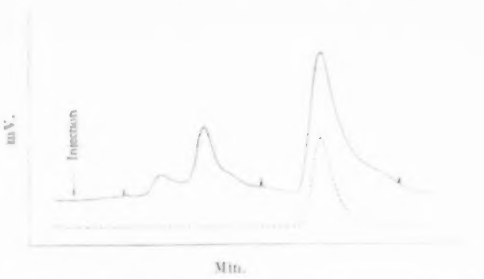

Fig. 1. Gas chromatographic (– – –) and radiochemical (——) analysis of crude, tritiated toluene. Carrier-free by-products, possibly hydrogenated toluenes, are detected from their radioactivity

The interaction of the reactive entities produced in this primary process ensures, among other reactions, an efficient tritium exchange including those cases where the organic compound does not exhibit absorption bands in the ultra-violet region. The application of the above technique to the preparation at tritiated toluene and *cyclo*hexane is briefly described. Table 1 summarizes the experimental conditions employed and the activity found in the pure, tritiated hydrocarbons.

A low-pressure model *NK* 20/40 Hanau resonance lamp was used for all the irradiations. A simultaneous gas-chromatographic and radiometric analysis of the crude toluene and *cyclo*hexane demonstrated the presence of several carrier-free radioactive by-products (Fig. 1).

An efficient radiochemical purification of the tritiated substances was achieved by preparative-scale gas chromatography. Columns 3 m. long, packed with di-*n*-decyl-phthalate on 'Celite *C*22' were employed, using nitrogen as carrier gas. The column temperature was 85° C. for the toluene and 70° C. for *cyclo*hexane.

The gas-chromatographic steps were repeated until a simultaneous mass and activity analysis failed to detect radioactive contaminants in the purified samples, the activities of which were measured in 250 ml. ionization chambers, connected to a vibrating-reed electrometer, as described by Wilzbach, Kaplan and Brown[9].

The results in Table 1 demonstrate that comparatively high percentages of the T_2 activity have been incorporated into the labelled compounds, including *cyclo*hexane, which does not absorb in the ultra-violet region.

To evaluate the efficiency of the present method, it may be pointed out that, with Wilzbach's technique, an activity of at least 500 mc. of T_2 must be employed to introduce the same tritium activity into pure toluene, in an equal exchange time. In this way, the higher efficiency of the mercury-photosensitized exchange method allows the preparation of labelled samples with a considerable saving of tritium activity and/or exchange period.

From the preliminary results obtained, it seems that the simple method described could be usefully employed as a general technique for the labelling of organic compounds.

Two mechanisms are conceivable to explain the mercury photosensitized exchange:

(1) Excitation and dissociation of gaseous tritium by $^3P_1$ mercury atoms, the energy of which is sufficient to dissociate the T_2 molecules; the tritium atoms can afterwards react with the organic substrate; (2) excitation and dissociation of organic molecules which can interact with tritium atoms or molecules.

More detailed information will be given later.

We are indebted to Prof. G. Giacomello for the helpful discussions.

This work has been supported by Comitato Nazionale Energia Nucleare.

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A 'Dry' Mounting Autoradiographic Technique for the Localization of Water-soluble Compounds

ONE of the disadvantages of the stripping film autoradiographic technique is that the film is floated on a water surface and apposed to the radioactive material by dipping the slide into the water and picking up the film so that its under surface (the emulsion layer) is in direct contact with the specimen. During this mounting procedure (called here the wet technique) and subsequent drying period, which may be several hours, there is opportunity for water-soluble compounds to diffuse out of the specimen, or to leave their original site and be absorbed elsewhere[1,2].

In an attempt to define the metabolic pathway of labelled precursors of deoxyribonucleic acid using either phosphorus-32 or tritium compounds, it became apparent that the soluble intermediates were, in fact, readily lost during the conventional autoradiographic procedures. The use of vacuum drying, freeze substitution or other methods of cell fixation did not prevent a considerable loss of phosphorus-32 from nuclei afterwards placed in aqueous solutions; autoradiographs of nuclei using these methods of fixation and the wet autoradiographic technique revealed some isotope definitely associated with nuclei, but much more was randomly distributed throughout the extranuclear portion of the smear. In some cases, there was relatively little radioactivity evident in the emulsion above the smear, but more encircling it, suggesting by the pattern that diffusion of isotope from the smear had occurred.

A direct mounting of dry, rectangular (1·5 × 3·5 cm.) strips of autoradiographic stripping plate (*AR*. 10) (Kodak, Ltd.) film emulsion to smears of nuclei from rat thymus glands on histological glass slides was achieved by the simple process of chilling the specimen in a refrigerator at 0–5° for 2–3 min., removing the specimens to the high humidity of the dark room, and immediately fixing the stripped emulsion to the specimen slide by firm even pressure with the thumb. It is assumed that the precipitation of a slight amount of moisture on the cold slide together with the pressure and warmth of the thumb permitted the firm bonding of the stripping film emulsion to the specimen and the slide which had been previously coated with gelatin ('subbed'[1,2]). Even without chilling the slide it was possible to mount dry emulsion to slides of nuclei by heavy thumb pressure although more artefacts were noted with this method.

To avoid the possibility of radioactive contamination of the specimen by the thumb, pressure can be applied to the dry film by means of a large cover-slip or another glass slide.

The direct 'dry' mounting gave rise to firm bonding of the film and specimen so that the film withstood photographic processing and staining procedures and remained tightly bound.

Rat thymus nuclei were prepared in ionic and sucrose media[3]. They were fixed either by rapid lyophilization in a desiccator or by freezing in *iso*-pentane at liquid-nitrogen temperature and dehydrating in ethanol at solid carbon dioxide temperature for 3–7 days[4]. The latter were mounted by allowing the slide to warm at room temperature for a minute or two until most of the alcohol had evaporated and then fixing the dry film emulsion directly to the smear with thumb or cover-glass pressure. The lyophilized smears were chilled and the emulsion similarly applied.

By this direct dry mounting technique we have been able to show the presence of phosphorus-32 mainly in the nuclei and less in the extranuclear area of the smear whereas the standard wet mounting procedure revealed a diffuse distribution of radioactivity throughout the smear regardless of whether formalin or Bouin's fixative, vacuum drying, freeze-substitution, oven (90°) or room temperature fixation was used. Autoradiographs of nuclei from rat thymus gland after intramuscular injection of ^{3}H-deoxycytidylic acid showed more emulsion grains over the nuclei at 10 and 30 min. after injection than did corresponding nuclei prepared by the standard wet mounting process. Redispersion of nuclei in ethanol after isolation in sucrose or ionic media and 'dry' mounting also resulted in a higher nuclear than extranuclear concentration of phosphorus-32 when compared to the oven or room temperature drying or vacuum dehydration followed by wet mounting. The resolution attained by the use of tritium was not impaired[5].

Attempts are now being made to apply the 'dry' mounting technique to tissues fixed and cut in the cryostat[6,7] and to those cut in the cryostat and dehydrated by freeze-substitution methods[4].

Since satisfactory autoradiographs have been obtained by this dry mounting technique, it is likely that the method may also prove useful in similar work with other cell components.

A more complete account of the results given by this method will be described elsewhere. Our thanks are due to the Rockefeller Foundation for financial

assistance and to the Commonwealth Fund for a research fellowship to one of us (P. J. F.).

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CHEMISTRY

Rates of the Reactions of Nitrogen Atoms with Oxygen and with Nitric Oxide

The reactions of nitrogen atoms with oxygen and with nitric oxide are of considerable interest, since whereas both processes (1) and (2) are exothermic:

$$N + O_2 = NO + O \quad \Delta H^\circ = -32{\cdot}8 \text{ kcal./mole} \quad (1)$$

$$N + NO = N_2 + O \quad \Delta H^\circ = -75{\cdot}1 \text{ kcal./mole} \quad (2)$$

the former reaction is very slow at room temperature, while the latter is extremely rapid. Kistiakowsky and Volpi[1] obtained a value of $2 \times 10^{13} \exp(-6200/\mathrm{R.T.})$ cm.^{3} mole^{-1}sec.$^{-1}$ for k_1 from a mass spectrometric investigation of the reaction between nitrogen atoms and oxygen molecules in a stirred reactor between 390° and 520° K. while a value of $1{\cdot}7 \times 10^{13} \exp(-7{,}500/\mathrm{R.T.})$ can be obtained from Kaufman's[2] work on the oxygen-sensitized decomposition of nitric oxide between 1,500° and 1,700° K. No direct determination of k_2 appears to have been reported, although values of 2×10^{11} (ref. 3) and a lower limit of 5×10^{12} cm.^{3} mole^{-1}sec.$^{-1}$ (ref. 1) have been recorded.

In the present work, we have studied the reaction between nitrogen atoms and oxygen molecules in the temperature range 412–755° K. Active nitrogen containing about ¼–½ per cent nitrogen atoms was produced by passing highly purified nitrogen through a 20 Mc./sec. electrodeless discharge. Active nitrogen flowed from the discharge through a 19 mm. internal diameter quartz reaction tube enclosed in an electric furnace. This tube had four sealed-in mixing jets spaced at 30-cm. intervals. Oxygen at known flow-rates was introduced at the first jet, and the decay of the nitrogen atom concentration along the tube was determined by titration of the nitrogen atoms at the three downstream jets, and at the first jet (before addition of oxygen). In the titration method[1,4–6] the end-point is observed as a sharply defined extinction point between the blue nitric oxide β-emission and the green air afterglow continuum with increasing nitric oxide flow-rate. This titration 'end-point' was taken to occur at the same nitric oxide flow-rate as the minimum current of a photomultiplier which observed the light emitted from the flowing gas downstream from the fourth jet. The nitrogen atom flow-rate was equal to that of nitric oxide at the end-point.

It was found that the rate of removal of nitrogen atoms was first order with respect to both nitrogen atom and oxygen molecule concentration and that two nitrogen atoms were removed for each oxygen molecule reacted, since reaction (2) is much more rapid than reaction (1). In this way a velocity constant of $8{\cdot}3 \pm 1{\cdot}0 \times 10^{12} \exp(-7{,}100 \pm 400/\mathrm{R.T.})$ cm.^{3} mole^{-1}sec.$^{-1}$ was determined for k_1 over the temperature-range 412–755° K. The rate constants calculated from this expression agree with the rates observed by Kistiakowsky and Volpi[1] and by Kaufman[2] to within the combined experimental errors of the observations.

At the higher temperatures used in our experiments and at high oxygen flow-rates (5–50 times the nitrogen atom flow-rate) a weak air afterglow spectrum was observed, and since this is known[7] to be due to the radiative process $NO + O = NO_2 + h\nu$, nitric oxide as well as oxygen atoms must be present in the reaction products. Under these conditions the rates of reactions (1) and (2) are more nearly comparable than at the lower temperatures and oxygen flow-rates used in the study of the kinetics of the overall reaction, and an appreciable amount of nitric oxide remains when all the nitrogen atoms have been consumed. The concentration of nitric oxide in the effluent gas was always less than 10 per cent of the initial nitrogen atom concentration, and it can be shown that in these circumstances the concentration of nitric oxide produced (y_0) is given by $y_0/b = k_1/k_2$, where b is the concentration of oxygen. The small amount of nitric oxide formed does not decay appreciably along the reaction vessel since the slow reaction (3):

$$NO + O + M = NO_2 + M \quad (3)$$

is followed by the rapid reaction (4) which regenerates NO from NO_2:

$$O + NO_2 = NO + O_2 \quad (4)$$

The amount of nitric oxide in the effluent gas (typically 0·05 per cent of the total flow) cannot be determined by conventional analytical techniques, and the following method was adopted. It is known that the intensity of the air afterglow is directly proportional to the concentrations of nitric oxide and oxygen atoms, and is independent of inert gases, and in runs where the oxygen flow-rate is varied the relative nitric oxide concentrations are given by the corresponding light intensities observed by the photomultiplier since the flow-rate of oxygen atoms produced is independent of the flow-rate of molecular oxygen used (always a large excess). The photomultiplier was calibrated to read directly in nitric oxide flow-rate by observing the enhancement of the light intensity when nitric oxide (diluted with nitrogen) was added to the reaction system at known flow-rates between the point of oxygen addition and the photomultiplier. For constant oxygen flow-rate, the photomultiplier current plotted against the flow-rate of added nitric oxide–nitrogen mixture gave a straight line, the slope of which was independent of oxygen flow-rate; and hence the small decay of oxygen atoms between the mixing point and the photomultiplier was roughly the same for all oxygen flow-rates used here. Making a small correction for the photomultiplier dark current, values of the effluent nitric oxide concentration (y_0) were thus obtained in runs where the flow-rate of oxygen (b) was varied. Plots of y_0 against b gave satisfactory straight lines with

slopes equal to k_1/k_2. Nitric oxide flow-rates down to 3 mgmoles/sec. were measurable with good accuracy by the technique described.

k_2 was determined as $3{\cdot}0 \pm 0{\cdot}6 \times 10^{13} \exp(-200/R.T.)$ cm.^{3} mole^{-1}sec.$^{-1}$ over the temperature-range 476–755° K. Thus, a direct determination of a velocity constant equal to about one-fifth of the bimolecular collision-rate has been made. The difference between the two frequency factors of reactions (1) and (2) appears to be greater than the combined errors of the determinations. This difference is of interest, since it cannot be explained on statistical grounds.

A full account of this work will shortly be submitted for publication. We thank the Department of Scientific and Industrial Research for a grant to one of us (M. A. A. C.).

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Use of the Mercury Drop Electrode Method for Direct Evaluation of Minute Amounts of Lead in Urine

For the diagnosis of the degree of lead poisoning the determination of lead in urine is very important although not easy. In the case of chronic poisoning the amount of lead in urine is not much larger than in normal urine samples, in which the lead concentration is very low (up to 80 γ/l.). Therefore the direct determination of lead in freshly voided urine without decomposition of the sample by ashing or by digestion with oxidizing acid is difficult. Some attempts have been made to overcome these difficulties and to determine lead without preliminary concentration, but they have not given satisfactory results.

Chmielowski and Myślak[1], who applied Teisinger's method for the determination of lead in blood[2] to urine samples, could indeed determine lead directly, but because of the insufficient sensitivity of the polarographic method, only in quantities larger than 500 γ/l. This renders it possible to estimate lead in cases of acute poisoning solely or when a patient is treated by means of calcium versenate. Similarly, direct electrodeposition of lead on to a platinum electrode from unprepared urine carried out by Cooksey and Walton[3] has not been widely accepted.

The application of the hanging mercury electrode method[4] to such a problem offers some advantages. High sensitivity and the possibility of concentrating selectively lead, while the concentration of other components remains unchanged, enabled us to develop a method of direct determination of very minute quantities of lead in urine.

The procedure is as follows: to the electrolytic cell which contains the hanging mercury drop electrode, salt bridge and small magnetic stirring bar, 10 c.c. of three times distilled water and 0·1 c.c. of specially prepared very pure concentrated hydrochloric acid were added. Oxygen was removed from the solution with hydrogen and then the preliminary electrolysis was carried out in an intensively stirred solution. During the electrolysis the potential of the cathode was kept constant at $-0{\cdot}7$ V. Stirring was stopped after 3 min. of concentrating electrolysis and the oxidation curves were recorded by means of a conventional polarograph polarized towards positive potential ($-0{\cdot}7$ to $-0{\cdot}2$ V.). In this way curves 1, 2 and 3 (Fig. 1) were recorded which show the degree of purity of the cell and added acid. A small minimum which appears at about $-0{\cdot}35$ V. corresponds to the oxidation of some traces of lead present in the acid and the electrolytic vessel. These traces can be determined by adding Pb^{2+} ions in such amounts that their concentration was 1×10^{-7} *M* (curves 4 and 5). Comparison of the curves 1, 2, 3 and 4, 5 shows that the concentration of Pb^{2+} ions in blank test solution was 5×10^{-9} *M*.

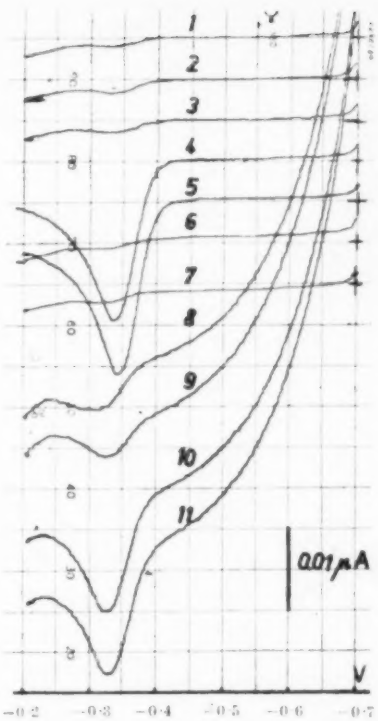

Fig. 1

Again the electrolysis of a new sample of acidified water was carried out to show that lead previously brought in was sufficiently removed from the cell (curves 6 and 7). After removing this test solution, 10 c.c. of the urine was placed in the cell and 0·1 c.c. of acid was added, and then deposition as well as recording were repeated (curves 8 and 9). Due to the reduction of various organic components of urine, the curves recorded in acidified urine differ from those obtained in the test solution of acid. However, at the oxidation potential of lead the curve is sufficiently flat to observe distinctly the oxidation minimum of lead (curves 8 and 9). Curves 10 and 11 were recorded after adding a known quantity of lead forming a

1×10^{-7} *M* solution. By comparing curves 8 and 10 it can be seen that the concentration of lead in urine was 5×10^{-8} *M*, that is, about 10 γ/l. The results obtained from twelve different 'normal' urine samples gave 10-3 γ/l. as a mean.

The oxidation minimum for lead corresponding to the same amount of the standard was much smaller in urine (curve 10) than in the acid (curve 4). This difference is caused by the greater viscosity of urine in comparison with the viscosity of the solution with acid added. The calibration curves describing the dependence of maximal intensity of oxidation curves on concentration of lead obtained for both solutions were linear, and this allows the use of the standard addition method.

These results show that lead can be directly and quantitatively determined not only in urine of persons poisoned with lead, but also in the 'normal' ones without any preliminary concentration and mineralization as a separate operation.

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Pyrazine-Metal Halide Complexes: New Types of Metal-Ligand Polymers

The compounds[1,2] of pyridine with metal salts have been well investigated, but little has been reported concerning the corresponding pyrazine (Fig. 1) compounds. Pyrazines have a second (potential) donor nitrogen atom in the 4 position and are much weaker[3] bases than the pyridines. (Pyrazine $pK_a = 1{\cdot}1$; *cf.* pyridine $pK_a = 5{\cdot}2$.) It appears to attach a proton, or to quaternize at one nitrogen atom only, the second being deactivated[4]. Condensed pyrazines, for example phenazine[5], have been studied, but only two simple pyrazine complexes, namely, tetracarbonyl-*bis*(methylpyrazine)-chromium(O) and the corresponding molybdenum(O) compound, appear to have been reported[6].

Our investigation springs from an interest in the relative donor capacities of the two nitrogen atoms towards metals, in the effect of substituents on donor capacity, and in the potential value of these complexes for the preparation of semi-inorganic (metal–ligand–metal) polymers. This communication summarizes certain novel reactions of pyrazine and its mono-, bi- and tetra-methyl substituted derivatives. We list in Table 1 some of the new complexes

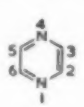

Fig. 1

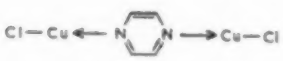

Fig. 2

Table 1

Metal ion	Complex	Physical form	C.N.*	Mag. mom. (B.M.)
Cu(I)†	(2 : 6-Di-Me-pyrazine)Cu_2Cl_2	Orange	2	0·0
	(2 : 5-Di-Me-pyrazine)Cu_2Br_2	Orange	2	0·0
	(Pyrazine)Cu_2I_2	Orange	2	0·0
	(Me-pyrazine)$Cu_2(CN)_2$	Yellow	2	0·0
	(Tetra-Me-pyrazine)$Cu_2(CN)_2$	Yellow	2	0·0
Ni(II)	(Me-pyrazine)$_4NiCl_2$	Pale green	6	3·31
	(2 : 6-Di-Me-pyrazine)$_2NiBr_2$	Yellow white	6	3·35
	(Me-pyrazine)$NiBr_2$	Green white	6	3·40
	(2 : 5-Di-Me-pyrazine)$NiBr_2$	Intense purple	4 ?	~0·0
	(2 : 5-Di-Me-pyrazine)$NiCl_2$	Green white‡	6	3·58
	(Pyrazine)$_2NiI_2$	Yellow	6 ?	3·23
Co(II)	(2 : 5-Di-Me-pyrazine)$CoCl_2$	Violet pink‡	6	5·53
	(2 : 5-Di-Me-pyrazine)$CoBr_2$	Dark blue§	4	4·68
	(Me-pyrazine)$CoBr_2$	Blue	4 ?	4·71
	(2 : 6-Di-Me-pyrazine)$_2CoI_2$	Deep green¶	4	4·76
	(2 : 6-Di-Me-pyrazine)$_2CoBr_2$	Violet pink	6	5·37

* C.N., Co-ordination number of metal ion.
† One of each type of complex only is quoted; several others with the five ligands have been prepared.
‡ Isomorphous.
§ Dimeric in 2 : 5-dimethylpyrazine solution; non-electrolyte in acetone.
¶ Monomeric in camphor; non-electrolyte in acetone and nitromethane.

of univalent copper and of bivalent nickel and cobalt. Unfortunately, the low solubility of most of these compounds in suitable solvents renders inapplicable many physical techniques which are diagnostic of structure; however, magnetic and spectroscopic data have proved specially valuable for this purpose.

Univalent copper gives rise to complexes in which there are *two* cuprous halide groups to each pyrazine molecule. The simplest structure for these complexes is shown in Fig. 2.

These represent the first complexes in which each nitrogen atom is bound to a metal atom. One is tempted to conclude that d_π–p_π bonding from the metal to the ligand could prove a means of increasing the negative charge on the ligand and hence of increasing the donor capacity of the second nitrogen atom. However, as will be discussed in a later communication, infra-red and other studies have led us to conclude that double bonding is probably less important than might have been expected at first sight.

Cupric complexes have been prepared, but these have not yet been studied in detail because their insolubility, coupled with a tendency to undergo reduction to the cuprous state, renders investigation of their structure rather difficult. Several different types of bivalent nickel compounds have been isolated. Complexes of the type ligand$_4NiCl_2$ are almost certainly six-covalent, and lose the ligand exceedingly readily, yielding complexes of the 1 : 1 type (see below). The 2 : 1 complexes (2 : 6-dimethylpyrazine)$_2NiBr_2$ and (pyrazine)$_2NiI_2$ achieve six-co-ordination through halogen bridging, and the 1 : 1 complexes (methylpyrazine)$NiBr_2$ and (2 : 5-dimethylpyrazine)$NiCl_2$ appear to reach the six-co-ordinate state by both halogen and pyrazine

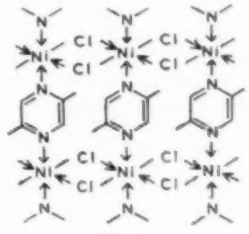

Fig. 3

bridging. A possible structure is illustrated in Fig. 3. These compounds are all paramagnetic with moments in the range expected for octahedral co-ordination (2·9–3·3 B.M.).

However, and in marked contrast, the purple (2 : 5-dimethylpyrazine)$NiBr_2$ is diamagnetic, a property generally associated (in the case of Ni(II) complexes) with a four-co-ordinate square planar or a six-co-ordinate tetragonal arrangement of the attached ligands. The behaviour is surprising in view of the fact that the corresponding chloro-derivative—this halide ion is usually assumed to give rise to a stronger ligand field than the bromide ion—is paramagnetic. Also the larger bromide ion is expected to cause greater steric interaction with the methyl group in a square complex than would occur in the chloro derivative. The chloro-complex is apparently octahedral six-co-ordinate, because it is isomorphous with the corresponding cobalt compound, the colour and magnetic properties of which strongly support octahedral co-ordination.

Of the bivalent cobalt compounds reported (2 : 6-dimethylpyrazine)$_2CoI_2$ is monomeric and its spectral and magnetic data point strongly to a tetrahedral arrangement. (2 : 5-dimethylpyrazine)$CoBr_2$, on the other hand, is dimeric, though evidently still tetrahedral, and probably has a structure involving bromine bridges. The high magnetic moments, and colour, of the remaining cobalt complexes listed suggest strongly an octahedral structure. Those of the 1 : 1 type evidently involve both pyrazine and halogen bridging (as Fig. 3), whereas (2 : 6-dimethylpyrazine)$_2CoBr_2$ involves halogen bridging only.

Infra-red spectroscopy has proved to be a most useful tool in the elucidation of the structure of these complexes further data on which will be reported in detail shortly.

We are indebted to the Wyandotte Chemical Corporation, Detroit, Mich., for the supply of pyrazines and for financial support.

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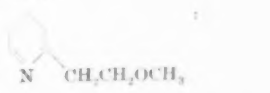
BIOCHEMISTRY

A New Anthelmintic with Unusual Properties

During studies on anthelmintic activity which have been in progress in these laboratories during the past few years, we have encountered an interesting degree of activity among a limited number of substituted pyridines. Nothing of practical value emerged from the early observations, but they caused us to retain an interest in related substances. Recently, through the courtesy of The Midland Tar Distillers, Ltd., we had the opportunity of examining some pyridine compounds made in their Research and Development Department, and one of them, prepared by Mr. P. Arnall, has proved of exceptional interest. This compound is 2-(β-methoxyethyl)-pyridine (U.K. Patent Application 40845/59; 40931/59; 20099/60):



It is a liquid and extremely soluble in water.

Using experimental infections in mice with *Nematospiroides dubius*, *Nippostrongylus muris* and *Heterakis spumosa* and following methods developed by our colleague Dr. D. G. Davey, it has been possible to investigate the anthelmintic activity of this compound against nematodes inhabiting quite different regions of the alimentary canal. *N. dubius* inhabits the duodenum, *N. muris* the ileum and *H. spumosa* the colon, and marked activity has been obtained against all these species. In our experience a compound having similar activity against the three species is extremely rare, though we think this is not due to specific resistance on the part of the worms but to differences in their habitat. Thus the resistance of *N. dubius* to many anthelmintics appears to arise because it is confined to the duodenum.

The feature which makes 2-(β-methoxyethyl)-pyridine unique in our experience is the observation (Table 1) that it is more active when administered subcutaneously than orally. We know that the compound is excreted into the alimentary canal, seemingly along the whole length, and possibly this allows more intimate contact with all worm species whatever their location.

Table 1. Comparative Activity of 2-(β-methoxyethyl)-pyridine, Phenothiazine and a Mixture of Bephenium Embonate and Hydroxy Naphthoate in Mice

	2-(β-methoxyethyl)-pyridine		Mixture of bephenium embonate (1/3) and hydroxy naphthoate (2/3) (oral)	Phenothiazine (oral)
	Subcutaneous	Oral		
(1) *H. spumosa*	360	560	1,054	800
Relative activity	1·0	0·64	0·34	0·45
(2) *N. muris*	350	450	440	2,012
Relative activity	1·0	0·77	0·80	0·17
(3) *N. dubius*	640	880	3,400	Approx. 14,000
Relative activity	1·0	0·73	0·19	0·05

The figures in the columns opposite the worm species give the dose in mgm./kgm. which is required for a 95 per cent reduction in worm burden.

Critical tests which will be reported in detail elsewhere have shown that 2-(β-methoxyethyl)-pyridine possesses greater activity against nematodes in mice than phenothiazine or a mixture of bephenium embonate (1/3) and hydroxy naphthoate (2/3), both of which are used in practice. Typical results are summarized in Table 1. Activity has also been demonstrated in mice against the immature forms of *N. dubius* and *N. muris*.

The results in mice with this compound were so promising that it was, and continues to be, tested in sheep, cattle and other domestic animals. Preliminary reports from various workers indicate that it may be of considerable value and, accordingly,

it is being given more widespread use under the Imperial Chemical Industries brand name 'Promintic'.

A. W. J. Broome
N. Greenhalgh

Imperial Chemical Industries, Ltd.,
Pharmaceuticals Division,
Alderley Park,
Macclesfield. Nov. 3.

A Pyroninophilic Component in Pathological Serum Proteins and Urinary Proteins

Pyronine-methyl green is frequently used in histological investigations for staining ribonucleic acid and deoxyribonucleic acid[1].

Yeoman[2,3] applied this staining method to serum proteins and urinary proteins from patients with multiple myeloma. In each of the 11 cases examined, the abnormal protein fraction stained red-violet with pyronine-methyl green after paper electrophoresis of both serum and urine. This staining reaction was negative in 100 cases of hyperglobulinæmia and proteinuria. Yeoman presumes that the staining is specific for true myeloma proteins.

For some considerable time, investigations in our laboratory have been aimed at the chemical and immunological characterization of paraproteins. Consequently we have at our disposal a collection of sera from patients whose blood plasma contains one or several abnormal protein fractions. In addition, a few Bence Jones proteins are available. The specificity of the above-mentioned staining was tested in this material. A sample of each serum and each Bence Jones protein was submitted to electrophoresis at *p*H 8·6 in agar gel[4], and then stained with pyronine-methyl green in an acetate buffer at *p*H 4·8.

Table 1. Staining of Paraproteins with Pyronine-Methyl Green

	Positive	Negative
Multiple myeloma	9	—
Bence Jones proteins	8	—
Waldenström's macroglobulinæmia	13	19
Atypical macroglobulinæmia	4	3
Unexplained paraproteinæmia	1	7

The results obtained (see Table 1) show that the abnormal serum protein fraction stained with pyronine-methyl green in all cases of myeloma. Eight different isolated and purified Bence Jones proteins likewise produced a positive reaction.

A positive staining reaction was found in about half the cases of Waldenström's macroglobulinæmia and of so-called atypical macroglobulinæmia[5].

Sera from patients with an unexplained paraproteinæmia failed to stain, with one exception.

Therefore, this staining is unfortunately not specific for myeloma proteins from serum and urine, although these proteins showed a positive staining reaction both in the series examined by Yeoman and in our own material.

It is remarkable, however, that only abnormal protein fractions from serum and urine can be stained with pyronine-methyl green. This stainability might be taken to denote the presence of ribonucleic acid or deoxyribonucleic acid in these pathological protein fractions.

In order to verify this, the ultra-violet absorption spectrum of the electrophoresis-spots of these fractions

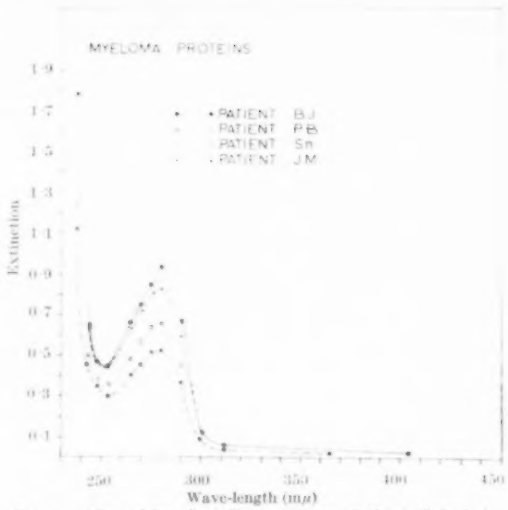


Fig. 1. Ultra-violet absorption spectrum of the pathological proteins in the serum of four myeloma patients

was determined. This proved to be identical with that of proteins; ribonucleic acid or deoxyribonucleic acid was not demonstrable in these fractions (see Fig. 1).

Both exposure to the influence of the enzyme ribonuclease (0·1 per cent in acetate buffer *p*H 6·0 at 37° C. for 30 min. and 7 hr., respectively) and treatment with 1 *N* perchloric acid at 4° C. failed to influence the stainability of the pathological protein fractions. The Feulgen reaction was also negative.

This warrants the conclusion that these proteins contain no ribonucleic acid or deoxyribonucleic acid.

Further investigations will be aimed at a definition of the component responsible for the positive staining reaction with pyronine-methyl green.

Thanks are due to Dr. D. Pragay for his kindness in supplying us with some Bence Jones proteins.

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Transferrin in Normal Cerebrospinal Fluid

Previous work has shown differences between some of the proteins in cerebrospinal fluid and those found in serum[1-3]. Thus paper-electrophoresis of concentrated normal cerebrospinal fluid may show a peak in the intermediate area between the beta- and gamma-fraction ('tau-fraction'), which is not seen in paper-electrophoresis of normal human serum[4-6]. The similarities and differences between transferrin in cerebrospinal fluid and in serum have been further investigated.

The cerebrospinal fluid was obtained by lumbar puncture from individuals without any neurological

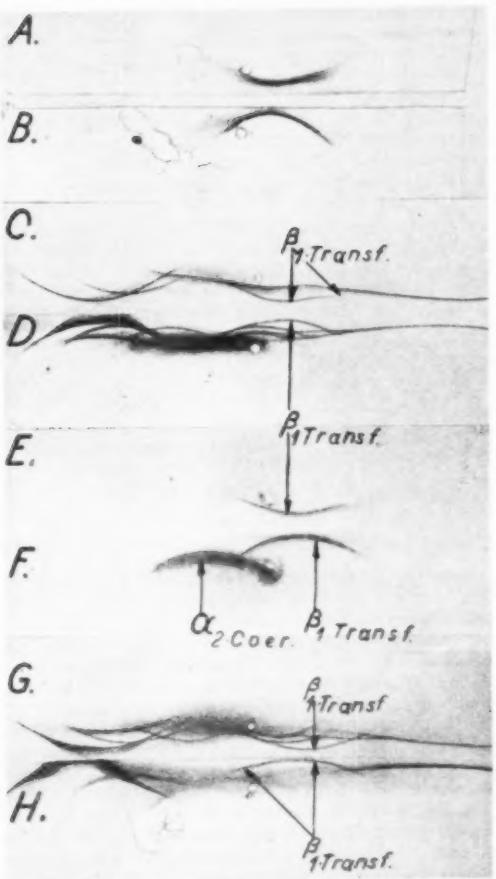

Fig. 1. *A*, Immuno-electrophoresis of iron-59 incubated cerebrospinal fluid, concentrated by pressure dialysis 50 times. The tracing is developed with a specific rabbit anti-transferrin antiserum. *B*, Immuno-electrophoresis of iron-59 incubated normal human serum, developed as *A*. *C* and *D*, The same as *A* and *B*, respectively, but now developed with a horse anti-human antiserum. *E* and *F*, The same as *C* and *D*, respectively, but now developed as autoradiogram. *G*, Immuno-electrophoresis of normal human serum developed as *C* and *D*. *H*, Immuno-electrophoresis of proteolytic digested normal human serum

disease. Care was taken to avoid any admixture of blood during the puncture. The fluid was concentrated by pressure dialysis and submitted to immuno-electrophoresis[3]. The development was performed with horse anti-human antiserum and specific rabbit anti-human transferrin, respectively.

A partial enzymatic digestion of normal serum proteins was achieved by means of pancreatic enzymes *NOVO*, possessing a proteolytic activity of 12 *NOVO* units/gm. = 600 Löhlein-Volhard units/gm.

The iron-binding capacity of transferrin and related proteins was demonstrated by autoradiography. 10–20 μl. of concentrated cerebrospinal fluid were incubated with about 10 μl. of a solution of radioactive iron-59 as ferric chloride; per sample 0·15 μc. was added with a specific activity of 5 mc./mgm. of iron. After incubation the serum was run immuno-electrophoretically and the plate exposed to a Kodak X-ray film.

The immuno-electrophoretic pattern of normal concentrated cerebrospinal fluid is shown in Fig. 1, and compared with that of normal human serum. The precipitation bow of transferrin from cerebrospinal fluid shows two differences from the corresponding bow of serum transferrin, indicating somewhat different physico-chemical properties of the two transferrins. The precipitation bow of cerebrospinal fluid transferrin has a double curvature and is more extended in the anode-cathode direction than the corresponding bow from serum. This extension is the result of a wider interval of mobility.

By incubation 2 ml. of human serum with 100 mgm. pancreatic enzymes *NOVO* at 37° C. for 1 hr. similar changes were found in the transferrin of this partially digested normal serum. Fig. 1 shows the immuno-electrophoretic tracing of such a proteolytically digested serum compared with that of genuine serum. No similar changes could be obtained from human sera treated with receptor-destroying enzyme (alias neuraminidase). In these experiments with the receptor-destroying enzyme several of the serum proteins showed a change in mobility, but not a reduplication of the immuno-electrophoretic bow. These changes in mobility are caused by a splitting off of the neuraminic acid[7].

The characteristic property of transferrin of binding iron was not qualitatively changed in cerebrospinal fluid. Fig. 1 shows the autoradiogram of an immuno-electrophoresis on concentrated cerebrospinal fluid incubated with iron-59. It is seen that the anodal as well as the cathodal part of the double-curved precipitation bow is able to bind iron. This figure, too, demonstrates the iron-binding capacity of normal human serum.

When the immuno-electrophoretic tracings of human serum are developed with a polyvalent horse anti-human antiserum not only transferrin but also coeruloplasmin was found to bind iron, and so was albumin when the maximal capacity of the two other proteins is surpassed (unpublished work).

In paper-electrophoresis on concentrated cerebrospinal fluid incubated with iron-59 the radioactivity could be traced to a maximum in the intermediate area between the beta- and gamma-fraction corresponding to the tau-fraction as seen by staining the paper for proteins with bromphenol blue.

No similar work on partial changes of the proteins compared with their normal carrier function is known to us.

One of us (J. C.) was in receipt of a grant from the National Multiple Sclerosis Society of Denmark.

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Methods for Determining the Rates of Catalase Synthesis and Destruction *in vivo*

Alterations in the amount of enzyme in a tissue can result from changes in the rate of synthesis or of destruction. The demonstration that 3-amino-1,2,4-triazole irreversibly inactivates catalase in the liver[1] without interfering with its resynthesis[2], and allyl-*iso*propyl acetamide blocks synthesis of new catalase[3] suggested that these compounds might be used as tools for studying the kinetics of catalase synthesis and destruction *in vivo*.

On injection of 3-amino-1,2,4-triazole, 1 gm./kgm. intraperitoneally, into rats there is a rapid fall in the liver catalase activity to a minimal value. After a lag period, during excretion of the aminotriazole, the catalase activity increases progressively over a period of 3–4 days, as originally described by Heim, Appleman and Pyfrom[4]. Experiments with radioiron have shown that this return of liver catalase activity results from the synthesis of new catalase[2]. Kinetic studies on the rate of catalase return following administration of aminotriazole show that the curve after the initial lag-period can be described by the equation:

$$C = \frac{k_S}{k_D}(1 - \exp(k_D t))$$

where C is the catalase activity at any time, t, and where k_S is interpreted as the rate of catalase synthesis, and k_D as the fraction of catalase destroyed in unit time.

In order to check the validity of the above interpretation, k_D, the first-order rate constant for catalase destruction, was determined by blocking catalase synthesis with allyl*iso*propylacetamide (we are indebted to Dr. W. E. Scott of Hoffmann–LaRoche, Inc., Nutley, New Jersey, for a generous gift of this compound). For the experiment one group of animals was given a single injection of aminotriazole, 1 gm./kgm. intraperitoneally; a second group was given allyl*iso*propylacetamide 200 mgm./kgm. twice daily intraperitoneally; a third group was given both drugs, and the fourth was used for controls. Five animals from each group were killed daily and the liver catalase assayed spectrophotometrically[5]. The results are plotted in Fig. 1. It can be seen that while the catalase activity of the aminotriazole group was rising, that in the allyl*iso*propylacetamide group was falling. The group of animals given both drugs was of particular interest, since it showed whether or not catalase synthesis had actually been completely blocked by the allyl*iso*propylacetamide. An early increase in catalase activity was observed to a low plateau of about 10 per cent of the normal value. This represents catalase which can be destroyed by aminotriazole, but the synthesis of which is not blocked by the allyl*iso*propylacetamide. This catalase is presumably in a different location within the liver cell from most of the liver catalase, or else is in cells other than the hepatic cells of the liver. Since this catalase may have different rates of synthesis and destruction from the main catalase fraction, it may create minor deviations from the theoretical curve for the return of catalase activity following aminotriazole.

Liver catalase synthesis and destruction *in vivo*

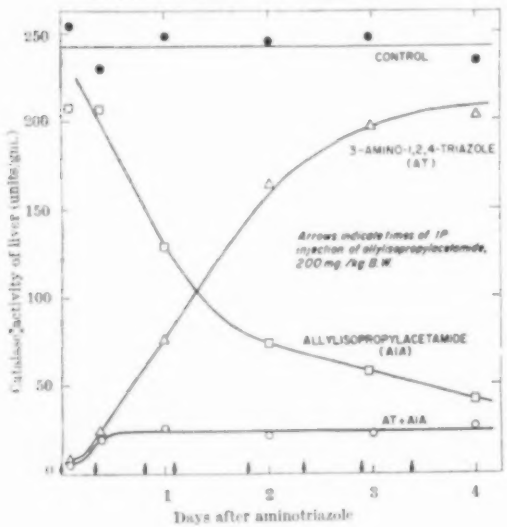

Fig. 1

Kinetics of liver catalase destruction *in vivo*

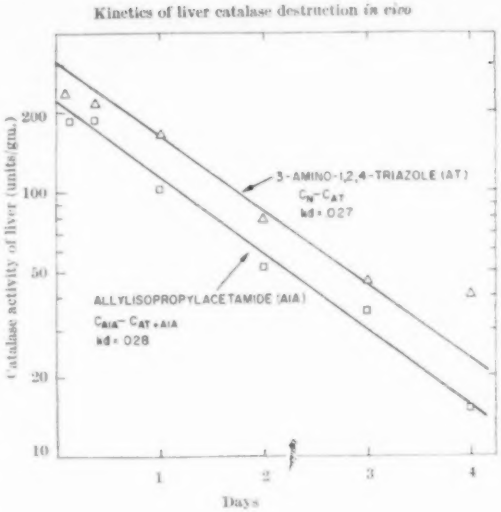

Fig. 2

If the rate at which the catalase activity of the aminotriazole group approaches the normal plateau is compared in a semilogarithmic plot (Fig. 2) with the rate at which the catalase activity of the allyl-*iso*propylacetamide group approaches its limit, which is the low plateau of the group given both drugs, it will be seen that two lines are obtained the slopes of which are nearly equal. The slope of these lines is equal to k_D, the rate constant for destruction. The rate constant for catalase destruction determined from the aminotriazole data is almost identical with that obtained when catalase synthesis is blocked with allyl*iso*propylacetamide. By substituting k_D in the equation: $k_S = k_D C_N$, where C_N is the catalase activity at the normal plateau, one can readily calculate k_S, the rate of catalase synthesis.

The above methods for studying the kinetics of catalase synthesis have the advantage that they are rather simple and require only injection of the drugs and assay of the liver homogenate for catalase activity. Only occasionally, to check the validity of a given system, does one need to use the radioisotopic methods, which require laborious purification of the enzyme to

a constant specific activity. These techniques should prove useful in determining whether the lowering of catalase activity in the liver during starvation[6], during tumour growth[7], and following injection of toxohormone[8] results from a decreased rate of catalase synthesis or an increased rate of its destruction. Experiments along these lines are under way.

The above investigation illustrates the usefulness of inhibitors of enzymes and of enzyme synthesis for kinetic studies on the rate of enzyme synthesis and destruction. Many other enzyme systems have been described where similar types of inhibitors are available. As these systems are being studied, it may be useful to carry out kinetic studies similar to those presented here.

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Formation of Hippuric Acid from Phenylalanine labelled with Carbon-14 in Phenylketonuric Subjects

Various authors have recently demonstrated the formation of hippuric acid from endogenous benzoic acid in the mammalian organism. Fasting humans[1] as well as humans and rats on a lactalbumin–carbohydrate diet[2] excreted hippuric acid, and its formation in the intact rat could not be inhibited by sulphasuxidine[2] or chloramphenicol[3]. Application of deuterium and phenylalanine labelled with carbon-14 resulted in labelled urinary hippuric acid[2–4]. In addition, when benzoic acid was isolated from the urine of human or rats fed benzoic acid, labelled with deuterium or carbon-14, the specific activity was about 20 per cent lower, indicating dilution by endogenous benzoic acid[4,5]. During the investigation of phenylalanine turnover in human phenylketonuria[6], I had the opportunity of studying the formation of hippuric acid from phenylalanine. Phenylketonuric subjects are characterized by their inability to convert phenylalanine to tyrosine to any significant extent. This results in an accumulation of phenylalanine and its keto derivative, phenylpyruvic acid.

Two phenylketonuric patients were subjects for this work. Their plasma phenylalanine concentrations were dietetically adjusted to 17·0 (patient K. H.) and 47·0 (patient R. S.) mgm. per 100 ml. 20 μc. of uniformally labelled phenylalanine-^{14}C, corresponding to about $7{\cdot}7 \times 10^6$ c.p.m., were injected intravenously into both patients after an overnight fast. All urine was collected for 6 hr.

The total amount of the urinary hippuric acid was determined by the photometric method of Komei[7]: to avoid inhibition by urea, the urine was first treated with urease. A hippuric acid standard was run in urine with every sample. The urinary hippuric acid was isolated by adding 1·0 gm. of non-isotopic hippuric acid and 50 gm. of neutral ammonium sulphate to 100 ml. of urine and acidifying with concentrated hydrochloric acid to *p*H 2·0. The resulting crude precipitate was recrystallized by dissolving in sodium hydroxide and heating in a boiling bath for 1–2 min. after the addition of a small amount of 'Norit'. After filtering, the *p*H was again adjusted to 2·0 with dilute hydrochloric acid and the solution placed in ice-water. This step of recrystallization was repeated once more. The hippuric acid was then repeatedly recrystallized from hot water until the melting point (189–190° C.) and specific radioactivity remained constant. This end-point was achieved when no chlorine ions were demonstrable with silver nitrate in the supernatant.

Hippuric acid isolated from patient R. S. was hydrolysed by refluxing with 6 *N* hydrochloric acid for 90 min. The hydrolysate was extracted several times with one volume of ether. The ether extract was cautiously evaporated on a steam bath and the residue taken up in a small volume of alcohol. The alcoholic extract was diluted with 10 vol. of water, whereupon crystals appeared, and cooled in ice for about 1 hr. The benzoic acid so obtained was recrystallized from hot water until melting point (121° C.) and specific radioactivity remained constant. In addition a solution of 60 μgm. of the purified benzoic acid did not demonstrate any colour formation with ninhydrin on filter paper. A comparison of the specific radioactivity of hippuric acid and benzoic acid in this patient gave 797 and 801 c.p.m. per mmole respectively. This indicates that only the benzoic acid part derived from phenylalanine and that there is no appreciable amount of radioactivity in the glycine side-chain.

Table 1 summarizes the findings. The absolute turnover-rate of free phenylalanine was calculated from the disappearance of the radioactivity from the blood plasma. These experiments and their results will be described in detail elsewhere. The calculation of the fraction of phenylalanine converted to hippuric acid was made assuming that all urinary hippuric acid derived from phenylalanine. Therefore, these values are only an estimate of the upper limit of hippuric acid formation from phenylalanine in phenylketonuric subjects. These upper limits are likely to be considerably lower for normal individuals.

Table 1

Name	L-Phenylalanine-^{14}C injected (c.p.m.) (*A*)	Hippuric acid excreted (m*M* per 6 hr.) (*B*)	Specific activity hippuric acid (c.p.m. per m*M*) (*C*)	Absolute turnover-rate of phenylalanine (m*M* per 6 hr.) (*D*)	$\frac{B}{D} \times 100$
K. H.	$7{\cdot}60 \times 10^6$	0·76	$2{\cdot}78 \times 10^6$	20·9	3·6
R. S.	$7{\cdot}76 \times 10^6$	1·27	$2{\cdot}36 \times 10^6$	22·1	5·7

Absolute turnover-rate as defined in (*D*) is the ratio of the total amount of free phenylalanine present in the body to the turnover-time of free phenylalanine.

$\frac{B}{D} \times 100$ is the percentage of phenylalanine leaving the free phenylalanine pool which is converted to hippuric acid.

since they possess the ability to convert phenylalanine to tyrosine and have, consequently, a higher absolute turnover-rate than phenylketonuric patients.

This work was supported by a research grant (No. 3691) from the National Institute of Mental Health, U.S. Public Health Service.

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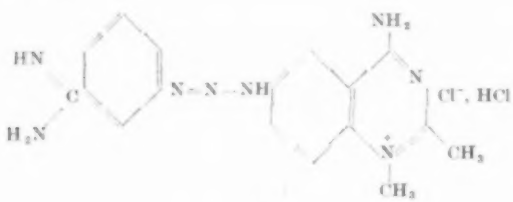
6-(*m*-Amidinophenyldiazoamino)-4-amino-1,2-dimethylquinazolinium Chloride Hydrochloride: a New Drug active against *Babesia canis*

As part of a study of diamidines which has extended over many years, we have recently screened for trypanocidal and babesicidal activity a number of compounds in which one of the amidine groups has been replaced by a cyclic amidine group. One of the most active of these is 6-(*m*-amidinophenyldiazoamino)-4-amino-1,2-dimethylquinazolinium chloride hydrochloride[1]:



(I)

(M. and B. 4986) (I). This compound, which contains the *m*-amidinophenyldiazoamino linkage present in the very active trypanocidal drug, *iso*metamidium[2], has babesicidal properties and is markedly active against *Babesia canis* in dogs.

The approximate maximum tolerated dose (subcutaneous) of M. and B. 4986 in healthy puppies was 25 mgm./kgm. body-weight, though marked tachycardia, accompanied by diarrhœa and vomiting, followed this dose, and persisted for about 1 hr. Fourteen days after a subcutaneous dose of 20 mgm./kgm. body-weight of M. and B. 4986 in adult dogs, there was no loss in weight, and no macroscopic signs of toxicity, apart from slight local skin thickening at the injection site, were observed on autopsy.

In therapeutic tests, a total of 46 puppies experimentally infected with *Babesia canis* were treated with doses of M. and B. 4986 between 0·5 and 10 mgm./kgm. body-weight. All the 12 infected puppies which received a subcutaneous dose of 2·5 mgm./kgm. survived, 3 were parasitologically negative within 24 hr., and all within 72 hr., 8 remained free of parasites for at least 30 days and 4 developed a parasitological relapse.

M. and B. 4986 (I) was prepared by coupling *m*-amidinobenzenediazonium chloride with 4,6-diamino-1,2-dimethylquinazolinium chloride. It was obtained as an orange crystalline solid, which decomposes at 237–238° C. (Found: N, 24·6; Cl, 15·3; H_2O, 11·4. $C_{17}H_{19}N_8^+,Cl^-,HCl,3H_2O$ requires N, 24·4; Cl, 15·4; H_2O, 11·7 per cent). It is approximately 0·5 per cent w/v soluble in water. In order to present a more soluble salt for field investigations the corresponding methanesulphonate (M. and B. 4986.A) has been prepared as orange crystals, decomposing at 205–208° C. (Found: N, 20·6; S, 12·0; H_2O, 3·4. $C_{17}H_{19}N_8,CH_3SO_3^-,CH_3SO_3H,H_2O$ requires N, 20·6; S, 11·7; H_2O, 3·3 per cent); it is approximately 25 per cent w/v soluble in water.

Further details, including a report on the field investigations, will be published in due course.

We thank Mr. D. J. Mellersh for his help with some of the biological work.

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PHYSIOLOGY

Excretion of Tryptophan Metabolites after Physical Effort

It has been shown that muscular effort is accompanied by the increased urinary excretion of one of the metabolites of tryptophan, namely, indoleacetic acid[1]. Pelikán and co-workers[2] have proved that there is increased excretion of another tryptophan metabolite, xanthurenic acid, after muscular effort.

Another tryptophan metabolite, 5-hydroxyindoleacetic acid, was then studied. The close relation between 5-hydroxytryptamine and the central nervous system is well known, and I wished to find out whether there is an increased urinary excretion of 5-hydroxyindoleacetic acid after muscular effort which is, moreover, often accompanied by considerable nervous tension.

5-Hydroxyindoleacetic acid is formed from 5-hydroxytryptamine by oxidase, and Sjoerdsma[3], Ressel[4], Udenfriend[5], de Gennes[6] and others state that its excretion is relatively constant. The normal urinary excretion of 5-hydroxyindoleacetic acid in men varies from 2 to 9 mgm./day[7]. Using a modification of Udenfriend's reaction, Schön and co-workers[8] recently found 1–6 mgm. (average 2·53 mgm./day). In the case of food only, the consumption of bananas results in increased excretion of this substance[9,10].

The urinary excretion of 5-hydroxyindoleacetic acid in men after various degrees of stress during athletics was followed. It was estimated in samples

of urine within 30 min. before and after muscular effort, its determination being carried out by the method of Sjoerdsma, Weissbach and Udenfriend[3].

Altogether 50 men, aged 19–50, were examined after muscular effort lasting from 5 min. to 3 hr. Twelve men ran an average of 1,250 m. for 5 min. at maximum effort on a laboratory treadmill. Eight men were examined after a 3-km. cross-country race and 21 men after a marathon race. Also included in the group examined were 9 football players after a football match.

In no case was sulphosalicylic acid proteinuria found before the effort. With the exception of 4 well-trained cross-country runners and 5 marathon runners, proteinuria could always be detected after the effort was made (ranging from slight turbidness to heavy protein precipitation). After a marathon race, proteinuria of 6–166 mgm./100 ml. (average value 47·1 mgm./100 ml.) was detected by means of Exton's method.

In no case, either before or after the effort, could any 5-hydroxyindoleacetic acid be detected. From this it can be concluded that, even when accompanied by considerable nervous excitement, muscular effort does not result in increased urinary excretion of this substance.

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Anionic Permeability of the Inhibitory Postsynaptic Membrane of Motoneurones

It has been postulated that the inhibitory postsynaptic potential in motoneurones is caused by the movement of ions across patches of the postsynaptic membrane that are momentarily (1–2 msec.) made very permeable for ions less than a certain critical size[1]. A sufficiently increased intracellular concentration of anions capable of passing through the postsynaptic membrane would change the normally hyperpolarizing inhibitory postsynaptic potential into a depolarizing one. In accordance with the hypothesis it was shown that injections of the small ions, Br^-, Cl^-, NO_3^-, and SCN^-, but not injections of the large HCO_3^-, $CH_3CO_2^-$, SO_4^{--}, $H_2PO_4^-$ or HPO_4^{--}, were effective in transforming the inhibitory postsynaptic potential into a depolarizing response. The diameter of the largest effective anion (derived from limiting ion conductances[2] and expressed relative to $K^+ = 1{\cdot}00$) was 1·11 and that of the smallest not effective, 1·65 (ref. 1). A weakness in the experimental evidence was the relatively few ions tested and the gap in size between the effective, and not effective, ions. Furthermore,

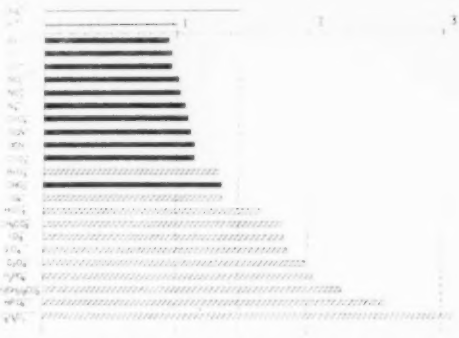

Fig. 1. The ions specified in the left column are arranged in order of hydrated ion size (derived from limiting ion conductances (ref. 2) and expressed relative to $K^+ = 1{\cdot}00$). The black bands indicate ions that are effective in changing the inhibitory postsynaptic potential into a depolarizing response; the hatched, those which are not effective. It should be noted that these results are consistent with the hypothesis that potassium ions can pass through the membrane but not sodium ions (ref. 1)

it was not possible to exclude a slight effect of the bicarbonate ion (diameter 1·65) (ref. 1).

We have now extended the previous investigation and tested 22 different species of anions. Microelectrodes containing the anion to be tested were inserted into motoneurones and used both for injection and recording. Most tests were made on knee flexor motoneurones that were inhibited by quadriceps group Ia afferents. The anions were injected by a steady current of $3–10 \times 10^{-9}$ amp. during 1 min. or more. The effect of the injection was judged by the polarity and size of the inhibitory postsynaptic potential immediately following the injection. The effects of the injections were always reversible within a few minutes after the injection. This recovery is attributable to the outward diffusion of the injected ions across the cell membrane.

The results are illustrated by the histogram (Fig. 1) showing the ions arranged according to their diameters. It appears that all ions with a diameter less than 1·32 (bromate) were effective in producing the reversible change of the inhibitory postsynaptic potential into a depolarizing response. Larger ions were ineffective except for the only slightly larger formate-ion (1·35). Injections of bicarbonate ions or carbonate ions never resulted in an immediate change of the inhibitory postsynaptic potential. After several injections of any of these ions there was often a gradual decrease of the hyperpolarization and finally a change to a depolarizing inhibitory postsynaptic potential. This late cumulative change is presumably due to secondary effects of these ions and cannot be taken as evidence for a similar action as that exerted by the small ions. Hence our findings support the hypothesis that the activated inhibitory postsynaptic membrane has an increased permeability for all anions less than a certain critical size.

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Lack of Uptake of Catecholamines after Chronic Denervation of Sympathetic Nerves

DENERVATION of sympathetically innervated structures has been known to cause supersensitivity of these organs to catecholamines[1] and depletion of these hormones[2]. However, no conclusive explanation has been offered for these findings. To clarify these phenomena further we compared the uptake of injected DL β-^{3}H-noradrenaline and DL β-^{3}H-adrenaline by intact and denervated tissue.

The right superior cervical ganglion was removed from cats, and sufficient time (more than 5 days) was allowed to elapse to ensure degeneration of the nerve fibres. The operated cats all had pupillary contraction and relaxation of the nictitating membrane on the denervated side. Tritium-labelled noradrenaline or tritium-labelled adrenaline was administered intravenously, 1 hr. later the animals were killed and the ^{3}H-catecholamine content was examined[3,4] in structures innervated by the cervical sympathetic nerve.

A striking reduction in the levels of ^{3}H-noradrenaline was observed in the chronically denervated structures (Table 1). Similar results were obtained after administration of ^{3}H-adrenaline. No differences were found in cats in which the right cervical ganglion was removed 15 min. before the administration of ^{3}H-noradrenaline. It is apparent from these results that the nerve endings or neighbouring structures take up and retain circulating catecholamines.

Table 1. EFFECT OF DENERVATION ON THE UPTAKE OF ^{3}H-NORADRENALINE AND ^{3}H-ADRENALINE

Tissue	Chronic denervation				Acute denervation	
	Noradrenaline		Adrenaline		Noradrenaline	
	Denervated	Innervated	Denervated	Innervated	Denervated	Innervated
External ocular muscle	5·9	47·9	1·8	15·4	24·9	26·6
Retractor bulbi muscle	1·9	11·3	1·8	8·2	13·2	13·4
Lachrymal gland	3·2	44·7	3·0	24·7	—	—
Salivary gland	5·7	42·4	2·5	115·8	75·5	88·6

In the chronic experiment the right superior cervical ganglia were removed from six adult male cats under pentobarbitone anæsthesia. After 5–21 days, 4 cats were given ^{3}H-noradrenaline and 2 cats ^{3}H-adrenaline (25 μgm./kgm. DL base, specific activity 3·25 mc./mgm.) intravenously under pentobarbitone anæsthesia. One hr. after the administration of the catecholamines the cats were decapitated and the ^{3}H-catecholamine content was assayed in denervated and innervated structures. In the acute experiment the right superior cervical ganglion from 2 cats was removed 15 min. prior to the administration of ^{3}H-noradrenaline. Results are expressed in mμgm. ^{3}H-noradrenaline or ^{3}H-adrenaline per gm. of tissue.

We have previously shown that binding is an important mechanism of catecholamine inactivation[3]. The present findings indicate that degeneration of nerve endings results in the inability to bind these hormones and consequently this mechanism of inactivation is inoperative. The effective concentration of unbound, active catecholamines in the vicinity of the receptors in denervated tissue would be expected to persist for longer periods, thus resulting in supersensitivity. Cocaine, which reduces the uptake of circulating catecholamines by the tissues[5], presumably by interfering with binding, also causes supersensitivity.

Removal of free catecholamines can also occur by enzymatic transformation. Catechol-O-methyl transferase[6] and monoaminoxidase[7] have both been considered to be involved in the metabolic inactivation of the catechol hormones. However, Burn *et al.*[8] have shown that inhibition of monoaminoxidase by iproniazid does not prolong the contraction of the nictitating membrane after stimulation of the sympathetic ganglion, whereas Wylie *et al.*[9] have demonstrated that inhibition of catechol-O-methyl transferase by pyrogallol prolongs the contraction.

From the results described here and elsewhere[3], inactivation of catecholamines at nerve endings and tissues is a complex process involving enzymatic transformation and binding. It appears that binding occurs primarily at the nerve endings and enzymatic transformation (presumably by catechol-O-methyl transferase) in tissue and at receptor sites.

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Effects of Pantothenic Acid (Calcium Pantothenate) and of Thyroxine on the Development of Chicken Embryos

IN earlier investigations, we have demonstrated[1] that the injection of 100 μgm. of calcium pantothenate into the yolk sac of chicken eggs after incubation periods of 4 and 10 days is responsible for an increase in body-weight, lasting 3–6 days. Together with the increase in body-weight, we have observed also an increase in tissue differentiation (studied by means of serial histological examination) especially of the nervous system (ganglia), kidneys, glandular stomach, liver and cartilages.

In the present work, eggs of White Leghorn–New Hampshire fowls, divided into four lots, were used. In the first lot 100 μgm. calcium pantothenate in sterile physiological solution (total volume of 0·1 ml.) was injected into the yolk sac after 4 and 10 days incubation. The second lot was injected with 5 μgm. thyroxine (Roche); the third with 100 μgm. of calcium pantothenate together with 5 μgm. thyroxine. The fourth lot (kept as control) was injected with 0·1 ml. of sterile physiological saline.

In six eggs of each group, embryonal life was interrupted after 7, 10, 13, 16, 19, 21 days of incubation for the eggs injected after 4 days incubation.

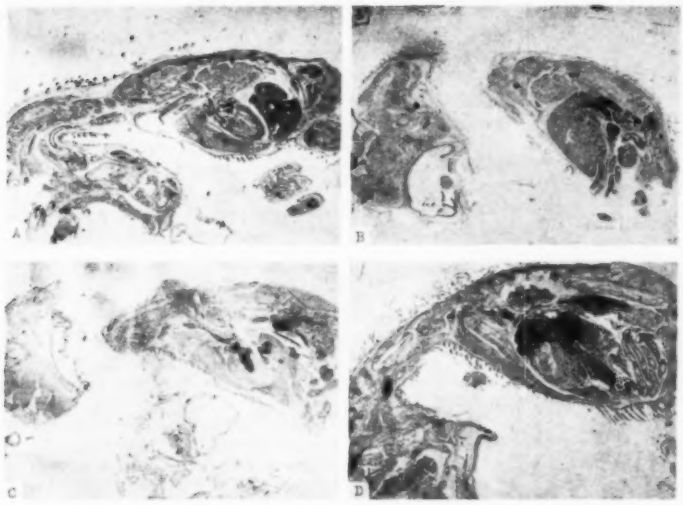

Fig. 1. Chicken embryos, tenth day of incubation, injected on fourth day. *A*, Control; *B*, thyroxine; *C*, calcium pantothenate; *D*, calcium pantothenate + thyroxine

For the eggs injected after 10 days incubation, embryonal life was interrupted after 13, 16, 19, 21 days of incubation.

All the embryos treated survived until the end of incubation. The embryos were weighed with all fœtal membranes after remaining in a refrigerator at 4° C. for 6 hr.

Our results may be summarized as follows: (1) Embryos treated with only 100 μgm. of calcium pantothenate show an increase in body-weight, which is more marked in the embryos injected after 10 days incubation, and lasting 5–6 days, as was demonstrated in our earlier work[1]. (2) Embryos treated only with a dose of 5 μgm. of thyroxine show, on the contrary, a reduction of body-weight, lasting from the day of injection until almost the end of embryonal life. (3) Embryos treated with calcium pantothenate together with thyroxine show a tremendous increase of body-weight compared to the controls, and still more striking if compared to the embryos treated with thyroxine alone. They are also bigger than the embryos treated with calcium pantothenate alone. This increase lasts until almost the end of embryonal life, for a longer period than that observed in the embryos treated with calcium pantothenate alone.

In Fig. 1 are shown examples of histological sections of 10-day embryos that give an idea of the effects of calcium pantothenate, thyroxine and thyroxine + calcium pantothenate on the body and on the tissues of the embryos treated.

The histological serial slides (which will be described in detail elsewhere) show clearly, in the embryos treated with calcium pantothenate alone and with thyroxine alone, a major, marked, differentiation of organic tissues, particularly evident in liver, nervous system, glandular stomach and cartilages. This increase in tissue differentiation is also very clear, and may be more marked, in the embryos treated with calcium pantothenate together with thyroxine.

In the light of these experimental results, it is possible to state: (*a*) that the pantothenic acid (calcium pantothenate) and thyroxine mutually increase, if injected together, their separate effects on organic tissue differentiation of developing chicken embryos; (*b*) that pantothenic acid prevents the well-known reduction of body-weight produced by thyroxine in chicken embryos; (*c*) on the other hand, thyroxine enhances the increase in body-weight produced by calcium pantothenate when that substance is injected alone.

The effects observed may be explained by the marked influence that pantothenic acid exerts on the intermediate metabolism, and particularly on protein synthesis, as a constituent of co-enzyme A.

It seemed of interest, therefore, to recall that de Franciscis and Landauer[2] have recently demonstrated in chicken embryos, of almost the same age as those we used, that cortisone and insulin exert different effects on the development of the embryos (micromielia, abnormalities, body-weight, etc.), when the two hormones are injected together or injected alone.

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Experimental Pre-Thrombotic State of an Organism resulting from the Dysfunction of the Physiological Anticoagulating System induced by an Atherogenic Diet

We have already shown[1–6] the existence in the animal organism of a reflex-humoral protective system which prevents the coagulation of blood circulating in the vascular system. In connexion with these results we became interested in the work of Wilgram[7,8] as well as in that of Thomas and Hartroft[9]. These authors have observed spontaneous myocardial infarctions in rats kept for several months on a diet enriched with fat and cholesterol. We supposed the diet indicated to produce a negative influence on the functional condition of the physiological anticoagulating system, due to which fact a pre-thrombotic state is seen to arise in the animal organism.

To verify this supposition, 100 adult male rats were transferred from a natural diet to that of Wilgram[7,8], supplemented with vitamin E in the form of an oily preparation from natural sources. Rats of the same age receiving a natural laboratory diet served as control. The functional state of the anticoagulating system in test and control rats was checked at various experimental stages by injecting thrombin or thromboplastin solution (preparation

from the rat brain) into the jugular vein. The experiment proved that the fat-cholesterol diet began to produce a negative effect on the functional state of the anticoagulating system 1½–2 months after its application, and in five and more months it blocked the activity of that system. Intravenous administration of moderate thrombin doses to such test animals causes their immediate death following intravascular clotting, in contrast with the control remaining alive after the same thrombin doses injected intravenously (Table 1). In all rats fed the experimental diet for five and more months the following changes were established: a rise in the concentration of fibrinogen (exp., 433 mgm. per cent; control, 312 mgm. per cent), a decrease of the blood fibrinolytic activity (exp. 7·5 per cent; control, 48·0 per cent), a sharp increase of the blood plasma tolerance to heparin (exp., 2 min. 25 sec.–6 min. 28 sec.; control, 7 min. 31 sec.–22 min. 48 sec.), and a ten-fold increase of the total cholesterol content in the blood (exp., 943 mgm. per cent; control, 95 mgm. per cent). It seems that a combination of the first three symptoms may be used to diagnose a pre-thrombotic state of the organism.

Table 1. Depression of the Function of the Physiological Anticoagulating System in Animals kept on a Prolonged Fat-Cholesterol Diet (Average Results)

Experimental conditions	Animal body-weight (gm.)	Thrombin dose* intravenously (ml.)	No. of animals		
			Total in the experiment	Survived	Died of thrombosis
Experiment: Rats kept on a fatty diet from 5 months to 7 months and 15 days	221–276	1·0–1·2	25	3	22
Control 1: Rats kept on a natural laboratory diet	223–276	1·0–1·2	25	22	3
Control 2: Rats kept on a fatty diet for 5 months. Thrombin inactivated by heating	251	1·7 inactivated	12	12	0

* Thrombin solution clotted an equal volume of oxalated blood in 5 sec. at 37°.

As a prophylactic against the formation of thrombi in test animals in a pre-thrombotic state a soybean trypsin inhibitor was used, as suggested by the results previously obtained[10]. The inhibitor preparation was isolated according to Künitz's method[11].

According to the results in Table 2 the trypsin inhibitor injected intravenously 5 min. before the thromboplastin injection has shown a good prophylactic action against thrombus formation.

Table 2. Protective Action of Trypsin Inhibitor against the Formation of Thrombi in the Case of Intravascular Injections of Lethal Thromboplastin Doses into Rats kept on a Fat-Cholesterol Diet for 5 Months (Average Results)

Dose of 5 per cent trypsin inhibitor solution intravenously (ml.)	Dose of thromboplastin (ml.)	Average animal weight (gm.)	No. of animals		
			Total in experiment	Survived	Died of thrombosis
Experiment (a fatty diet)					
1·4	2·1	264	10	10	0
Control (a fatty diet)					
6	2·1	253	10	0	10

The experimental results obtained by us indicate that the development of the myocardial infarction in rats fed the atherogenic diet of Wilgram[7,8] and of Thomas and Hartroft[9] is connected with the appearance in the test animal of a pre-thrombotic state resulting from a depression of the function of the physiological anticoagulating system.

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HÆMATOLOGY

Haptoglobin and Transferrin Types in the Kuru Region of Australian New Guinea

Kuru is a rapidly progressive and fatal neurological disease found to occur with high frequency among the Fore natives in the Eastern Highlands of New Guinea. Their tribal area, of several hundred square miles, is in a remote and rugged part of the highlands which has only recently become accessible to Europeans. Between 20,000 and 30,000 people live in the area affected and, of these, about 1 per cent is afflicted with the disease at any one time. Altogether kuru is responsible for more than half the deaths of Fore females and about 10 per cent of males. Extensive studies have as yet failed to reveal evidence of any environmental or nutritional factor involved in the production of kuru[1]. The possibility of the Fore people having a genetical predisposition to kuru was first mentioned in 1957[2]. Shortly afterwards, when a preliminary genetical study had been made, distinctive family patterns were found[3,4], and it was then suggested not only that the disease had an important familial component but also that this was quite possibly based on a single gene locus. The genetical hypothesis, advanced tentatively, was that kuru is under the control of autosomal alleles *Ku* and *ku* such that in females the homozygotes *KuKu* and heterozygotes *Kuku* are early- and late-onset victims, respectively, while in males the homozygotes *KuKu* are kuru victims but the heterozygotes are clinically normal. There are obvious weaknesses in basing inferences on genealogical data obtained from such primitive people through pidgin-English-speaking native interpreters. At the present time, however, this is the only way in which such material can be obtained. Nevertheless, it must be noted that the genealogical data gathered from many different parts of the affected region in extensive field studies during the past two years all exhibit essentially the same distinctive family patterns[5].

A puzzling observation has been Curtain's[6] reported association of kuru with the haptoglobin gene Hp^2. Using starch-gel electrophoresis, he found that the frequency of the Hp^2 gene in 54 kuru patients was 61 per cent as against only 36 per cent in 62 'normal' Fore individuals. Because this statistically significant difference seemed hard to reconcile with the genetical interpretation for kuru, an independent test for this association has been carried out. Blood samples were obtained by venepuncture from kuru patients and also from healthy Fore natives who were the parents of young female and male victims of kuru. Such parents, though not having any of the clinical symptoms of kuru, would be genetic carriers of the disease according to the above hypothesis. The samples were collected into Bayer venules and flown to Australia in ice-cold flasks. Haptoglobin typing of the sera was carried out in Perth using the vertical method of starch-gel electrophoresis as described by Smithies[7]. The results obtained are shown in Table 1.

Table 1. Haptoglobin Group Frequencies

	No. tested	Haptoglobin group 1—1	1—2	2—2	Gene frequency Hp^1	Hp^2
Kuru patients	47	21	20	6	0·66	0·34
Others	35	16	15	4	0·67	0·33
Total	82	37	35	10	0·66	0·34

The chief point which emerges from the present work is that there is no indication of any difference between the frequencies of the haptoglobin types in kuru patients and in those other Fore natives chosen for comparison. Furthermore, the frequencies of the Hp^1 and Hp^2 genes in both these groups are very similar to those reported by Curtain, not for his kuru patients, but for his control group of 'normal' individuals.

Several points of interest arise when the present results are compared with those reported for other populations. In this material, there is no Hp 0-0 individual nor is there anyone of the modified Hp 2-1 phenotype. These two types, which seem to be common in African Negroes[8], are rare in Europeans and in Japanese[9], Indian, Chinese and Malayan samples[10]. Neither type has been found in 89 Australian aborigines from South Australia, and there was only one 0-0 in a sample of 131 aborigines from the Western Desert (unpublished observations). The high frequency of the Hp^1 gene in this material is of interest. It is slightly higher than the frequency of 0·63 which has been reported for Micronesians of the Marshall Islands[11], and it is close to the highest value yet reported, namely, 0·72 for African Negroes. These values are much higher than in any of the series of South East Asian peoples so far tested[10], and they are in marked contrast to the low value of about 0·13 for the Hp^1 gene frequency found in Australian aborigines from South and West Australia—although a frequency of 0·64 for Hp^1 has been reported by Budtz-Olsen[12] for 100 aborigines from Central Australia, based on determinations using electrophoresis on paper.

The frequencies of the transferrin differences, typed simultaneously with the haptoglobins during starch-gel electrophoresis, are shown in Table 2. It is of interest that the frequency of the TfD_1 variant is the highest that has yet been reported, in published work, for any population. However, recent unpublished work in our laboratories indicates that it has an even higher frequency in Australian aborigines and that it is common also in the Veddahs of Ceylon.

Table 2. Transferrin Group Frequencies

	No. tested	Transferrin group CC	CD_1	D_1D_1	Gene frequency C	D_1
Kuru patients	45	39	5	1	0·92	0·08
Others	35	26	8	1	0·86	0·14
Total	80	65	13	2	0·89	0·11

For both the haptoglobin and transferrin types, the observed genotypic frequencies shown in Tables 1 and 2 are in close agreement with those expected with random mating.

We are indebted to the Administration of Papua and New Guinea, the Rockefeller Foundation and the University of Adelaide for financial assistance in connexion with this work.

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Hæmoglobin E in Egypt

Hæmoglobin E is generally thought to occur exclusively among people of Mongoloid origin; the greatest incidence being in the Burmese[1], Siamese[2], Cambodians[3], Indonesians[4] and Malayans[5]. The occurrence of hæmoglobin E in other peoples, for example, the Eti-Turks, an Arabic-speaking group living in southern Turkey[6], is usually accompanied by definite historic or familial ties with the South Eastern Asian. The discovery of hæmoglobin E in Egypt among a family which, so far as could be determined, has no direct relationship to the Asiatic (Mongoloid) is now reported.

The propositus was a 39-year-old male. The faces of the subject and two of his brothers and a niece who were seen are not those of the typical Arab. They represent, however, the features encountered among average Egyptians. Histories taken from the parents of the propositus revealed that the family had resided in the Nile Valley (delta) for many generations and had always gained a living as agricultural workers (fellaheen).

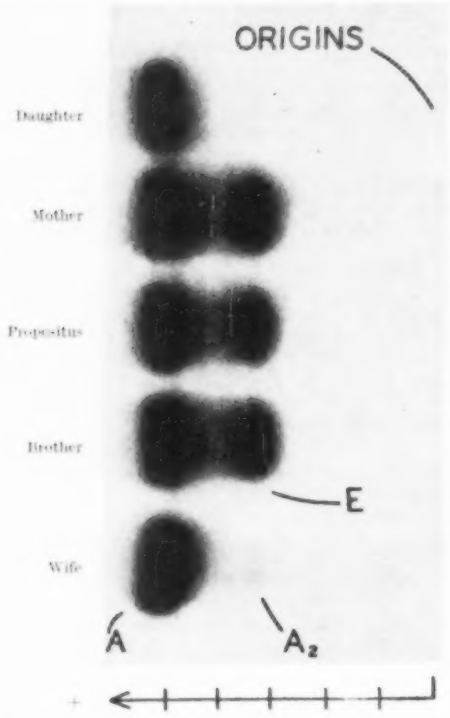

Fig. 1. Photograph of an unstained starch-gel slab after electrophoresis of haemolysates from members of a family having the haemoglobin E trait. Electrophoresis at 7 V. per cm. for 16 hr. Non-continuous buffer system (*tris*-maleate, 0·07 *M*, *p*H 8·7, for gel mixing; and borate, 0·3 *M*, *p*H 8·7, for bridge solution)

Twelve members of the family were examined. Nine were detected by starch-gel electrophoresis[7] to be haemoglobin E heterozygotes. Consistent with previously reported results[8], we found no haematological or radiographical evidence of haemolytic anaemia. A photograph of a starch-gel slab in which the haemolysates of the propositus, his mother, wife, child and brother were submitted to electrophoresis is shown in Fig. 1. Of the family members studied, only the wife of the propositus (a second cousin on the maternal side), her brother and a daughter were free of haemoglobin E. The concentration of the abnormal pigment was greater than 29 per cent in all cases.

It is interesting to speculate on the origin of haemoglobin E in Egypt.

(1) *Origin by mutation.* Although it is difficult to establish unequivocally, the probability of gene mutation must be considered in distal occurrences of abnormal haemoglobins. In this instance, we have demonstrated haemoglobin E in persons who reside at great distances from its assumed focus and who are considered of a different race.

(2) *Origin as a new haemoglobin.* Haemoglobin E in the Asiatic and that reported here might arise from independent genetic mechanisms. Although standard identification tests did not vary from previously published results, we were able to derive some differences in migration-rates between haemoglobin E and A_2, when the two were subjected to starch-gel electrophoresis in the second dimension. This is being studied further.

(3) *Origin by racial ties with Mongoloids.* This need scarcely be considered in the light of known anthropological differences between the two groups.

(4) *Penetration of haemoglobin E gene.* This is the most attractive possibility, provided gene mutation is not the prime factor. It is indeed reasonable to harmonize the presence of haemoglobin E in people of the Middle East with its existence among the Mongoloids of south Asia. It is in these areas and among these people that Islam was established in the Far East. Brumpt *et al.*[3] direct attention to the fact that in Cambodia there was something more than a coincidental increase of haemoglobin E among natives of the Muslim faith. Another factor, of course, would be the Mongol invasions of the Middle East in A.D. 1258. Their attack extended as far as the eastern border of Sinai. They dominated the area of Syria and Iraq for decades. Most probably it was during one of these historical events that the gene of haemoglobin E passed into the family we have examined.

The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the U.S. naval service at large.

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PATHOLOGY

Immunological Cross-Reactions between Salk 'Altered' Monkey Heart Cells and Ehrlich Ascites Carcinoma Cells

Recent work[1] has shown that the metabolism of Ehrlich ascites carcinoma cells (EA cells) can be inhibited by small quantities of specific antiserum in the presence of complement. We have now observed that antisera prepared against the Salk 'altered' monkey heart cells (MHS cells)[2] show activity not only against the homologous cells, but also against Ehrlich ascites carcinoma cells and HeLa cells as well.

Antisera were prepared in rabbits as described in a previous communication[1]. The sera were lyophilized immediately after preparation and used without inactivation, unless otherwise specified. The methods of incubation and analysis were identical to those described previously[1].

Table 1. Effect of Antisera on Different Cell Lines

Cells	Additions (antisera)	Uptake (c./min. /mgm. dry weight)	Incorporation (c./min./mgm. protein)
MHS	Nil	1,360	100
	MHSAS	710	68
	EAAS	1,320	106
EA	Nil	3,140	144
	MHSAS	140	69
	EAAS	176	25
HeLa	Nil	2,060	48
	MHSAS	147	3
	EAAS	1,750	36

Glycine 2 μM, at 45×10^3 c.p.m./ml. Aerobic incubation for 1 hr. in Krebs-Ringer phosphate. Gas phase, oxygen.

Table 2. Effect of Different Sources of Complement, using Salk 'Altered' Monkey Heart Cell Antiserum and Ehrlich Ascites Carcinoma Cells

Additions	Uptake (c./min./mgm. dry weight)
Nil	2,200
Normal fresh rabbit serum	2,200
Normal fresh guinea pig serum	2,040
MHSAS inactivated	1,890
MHSAS inactivated + fresh guinea pig serum 1 : 1	1,730
MHSAS inactivated + fresh rabbit serum 1 : 1	1,100
Lyophilized MHSAS	420

Conditions as in Table 1.

Table 3. Effect of the Alteration of the Cell-Serum Ratio

MHS cells (mgm. dry weight)	MHSAS (ml.)	Incorporation (per cent inhibition)	Uptake (per cent inhibition)
5·7	0·2	79	62
	0·1	37	17
	0·05	0	10
2·85	0·2	97	88
	0·1	54	43
	0·05	29	0
1·9	0·2	100	93
	0·1	75	75
	0·05	31	0

Conditions as in Table 1.

Conditions of the experiments were as follows: The incubations were carried out in Krebs–Ringer bicarbonate medium (Tables 1 and 3) or Krebs–Ringer phosphate medium (Table 2) under aerobic conditions for 1 hr.

The constituents per 1 ml. were:

Test serum	0·1 ml.
Complement (where applicable)	0·1 ml.
Glycine-1-^{14}C, 45×10^3 c.p.m.	2 μmoles
Glucose	10 μmoles
Cell suspension	0·5 ml.

The dry weight of the cell suspension was 4·0 mgm. unless otherwise indicated.

The results are expressed as follows: (*a*) uptake: counts/min./mgm. dry weight of cells; (*b*) incorporation: counts/min./mgm. protein.

The results presented in Table 1 show that, while Salk 'altered' monkey heart cell antiserum markedly affects the uptake and incorporation of glycine-1-^{14}C by the Ehrlich ascites carcinoma cells and HeLa cells as well as by the Salk 'altered' monkey heart cells, the Ehrlich ascites carcinoma cell antiserum (EAAS) is much less effective against the heterologous cells.

We have also observed, as indicated in the previous report[1], that the reaction is dependent on the presence of complement. Inactivation of the antiserum at 56° C. for 30 min. brings about a loss of inhibitory activity. The conventional source of complement, namely, guinea pig serum, restores little of the inhibitory activity. Normal fresh rabbit serum is much more effective, but unheated (lyophilized) antiserum is always the most effective inhibitor. Table 2 shows the results of a typical experiment illustrating this phenomenon.

Since it was known from previous experiments (unpublished results) that with the Ehrlich ascites carcinoma cells and the homologous antiserum there is a ratio of cell to antiserum at which maximal inhibitory activity is observed, the effects of changing the cell/antiserum ratio with the Salk 'altered' monkey heart cells were considered.

The results in Table 3 indicate that the inhibition observed at a given concentration of serum is much greater when few cells are used.

Recently, Defendi and Colter[2] observed immunological cross-reactions between different cell lines. Our results, using different techniques, indicate that such cross-reactions exist between Ehrlich ascites carcinoma cells, Salk 'altered' monkey heart cells, and HeLa cells; thus antisera against the Salk 'altered' monkey heart cells also inhibit the metabolic activity of the Ehrlich ascites carcinoma cells and HeLa cells. However, antiserum against Ehrlich ascites carcinoma cells does not affect the Salk 'altered' monkey heart cells to the same extent.

Further experiments are required using cross-absorption techniques to decide which cell fractions are responsible for this phenomenon.

We are indebted to the Connaught Medical Research Laboratories, Toronto, for having made the Salk 'altered' monkey heart cells available to us. This work was supported by a grant from the National Cancer Institute of Canada and the National Research Council of Canada. We are grateful for the help and encouragement given by Profs. J. H. Quastel and R. W. Reed.

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Inhibition of Experimental Cirrhosis by Carbon Tetrachloride following Treatment with Aminoacetonitrile

Experiments on lathyrogenic compounds have shown that they exert a delaying action on collagen formation[1–4]. The mechanism by which they act is still unknown.

Owing to the biological interest of these findings, and in view of their possible pharmacological implications in those pathological conditions where the new formation of collagen is the fundamental lesion or a most important component of the pathological picture, the present experiments were carried out in order to study the action of aminoacetonitrile (AAN), one of the lathyrogenic agents, on experimental cirrhosis by carbon tetrachloride.

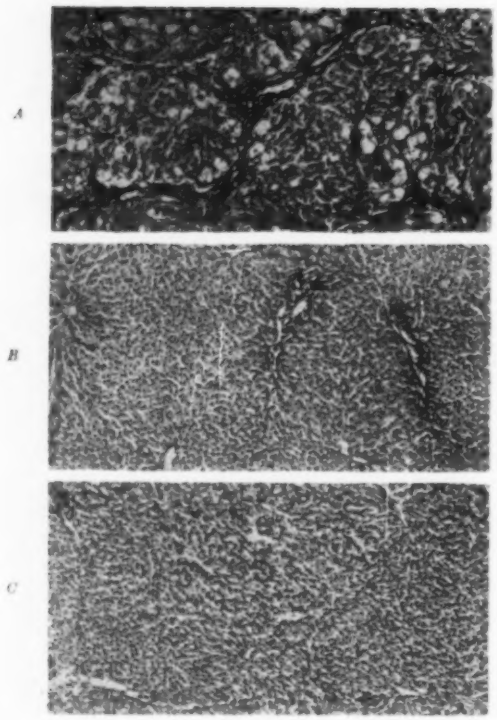

Fig. 1. *A*, Rat liver after 60 days of treatment with carbon tetrachloride; *B*, rat liver after 60 days of carbon tetrachloride and 53 days of AAN treatment; *C*, normal rat liver. Van Gieson staining. (× c. 31)

100 female rats weighing 150–200 gm. were used. Cirrhogenic treatment was given daily by inhalation, all the animals simultaneously breathing the same atmosphere with carbon tetrachloride vapour.

The cages containing the animals were put into a box where carbon tetrachloride was allowed to fall in drops on the plate of an electric oven until the vapour reached an approximate concentration of 50 gm. per m.^{3}. The dropping velocity was regulated so that this concentration of carbon tetrachloride vapours was attained after 7–8 min. Immediately after, the cages were removed from the box.

After the first week's treatment with carbon tetrachloride the rats were divided into two groups of equal number. One group was treated daily, in addition to carbon tetrachloride, with a subcutaneous injection of 20 mgm. aminoacetonitrile hydrosulphate dissolved in 0·2 ml. water and neutralized with sodium hydroxide. The other group, used as control, continued to receive daily treatment with carbon tetrachloride. After one month, at varied intervals, an equal number of animals from the two groups were killed and liver sections were histologically examined, having been stained with Van Gieson, Azan Mallory, hæmatoxylin and eosin. After two months the experiment was ended by killing all the surviving animals.

Both in the group treated with carbon tetrachloride and in that treated with carbon tetrachloride and AAN a high rate of mortality was observed, probably due to excessive amounts of the carbon tetrachloride used. Starting from the thirtieth day of treatment with carbon tetrachloride, livers were examined histologically, when possible, also from animals which were found dead.

Histological examination of the liver was carried out on a total of 25 animals treated with carbon tetrachloride and 24 animals treated with carbon tetrachloride and AAN. Between the thirtieth and fortieth days of carbon tetrachloride administration the newly formed connective tissue begins to be evident in the liver of animals treated with carbon tetrachloride alone, being detectable around the blood-vessels and in trabeculæ projecting among the lobules. From this moment the newly formed connective tissue is progressively increasing. After the sixtieth day's treatment, the cirrhosis picture is well marked. Big connective trabeculæ rich in fibroblasts and histiocytes surround the lobules, in which parenchymal cells show the typical severe alterations which follow carbon tetrachloride treatment (Fig. 1*A*). At this stage cirrhosis reveals itself macroscopically too, in that the liver acquires a clearly granular surface. On the contrary, in the liver of all the animals treated with carbon tetrachloride and AAN, including those which had received carbon tetrachloride for 60 days, the formation of collagen is extremely reduced: in comparison with the normal liver (Fig. 1*C*) it is slightly increased almost exclusively around the blood-vessels (Fig. 1*B*). Parenchymal cells are apparently normal.

The number of fibroblasts and histiocytes is also greatly reduced: this result does not agree with those of previous investigations[1–4] in which the action of lathyrogenic agents on the development of connective tissue was studied in different experimental conditions. It was then observed that lathyrogenic agents exert a delaying action on collagen formation, but do not inhibit the multiplication of fibroblasts and histiocytes. The present observations would suggest that the inhibitory effect of AAN on hepatic fibrosis due to carbon tetrachloride is not only due to the already known specific inhibition of collagen formation, but also to an inhibition of fibroblast multiplication.

Since the present observations do not exclude the possibility that AAN by some unknown interaction with carbon tetrachloride may prevent the latter substance from exerting its cirrhogenic activity, experiments are being made to ascertain whether it inhibits also fibroses of the same organ arising from other causes.

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ANATOMY

Continuous Regeneration of the Dentinal Nerve-Endings

In recent years several investigators have reported that nerve fibres have been observed growing from the dental pulp into the so-called predentine[1–5]. These authors all dealt with human dentine. I published[6] last year an account of work showing the presence of unmyelinated nerve fibres in the

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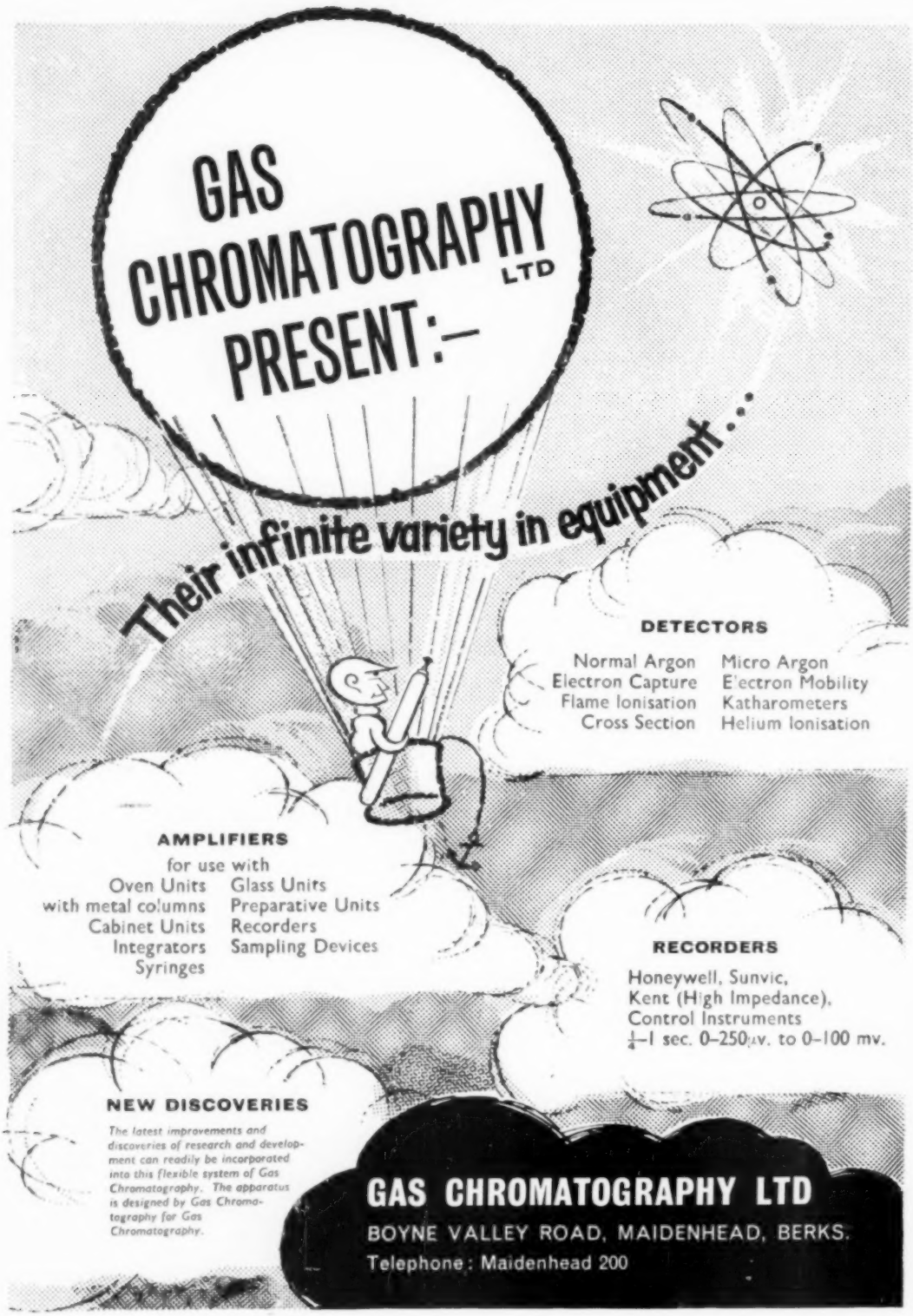
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predentine and the tubules of the dentine also of the rat. The occurrence of these fibres in rat dentine is very irregular, and seemingly certain spots are preferred. The distribution of the sensory nerves in the higher mammals is very similar, with the exception, of course, that the pulp innervation of the continuously growing incisor[7], and other continuously growing teeth[8] of rodents follows a quite different pattern. I have examined freshly extracted young human teeth also, demonstrating the nerve fibre in the dentine by the slightly modified method described by Romanes[6] using frozen sections. I found, in agreement with Weddel and Zander[9], that *p*H and length of time in the different fluids are of importance.

In some preparations I could clearly observe and confirm the presence of nerve fibres, mostly in the predentine, and also in some specimens the presence of a widely distributed nerve net in the predentine. The nerve fibre cannot be followed regularly in the calcified dentine by the methods of Romanes or Holmes; apparently this is possible only in very rare instances, as in the case of Powers[3]. I could follow some nerve fibres for a short way at the border of the calcified dentine, where they become indistinct. It seems to me that in the calcified dentine there are incorporated nerve fibres which are rarely distinguished with our present techniques. There is a possibility also that they become calcified and cease to function as receptors.

The dentine of higher mammals develops during the so-called functional period of the tooth also; the dentine becomes thicker and the pulp chamber narrower. The greater part of the dentine becomes calcified, although the inner—newly developed ground substance—is for a while uncalcified. This mechanism goes on until the formative power of the odontoblasts is exhausted. On the outer border of the uncalcified dentine, calcification goes on—spreading mostly in a spherical arrangement—and on its inner border new collagen ground substance is laid down.

I found that in the crown-pulp of human teeth the distribution of the unmyelinated nerve fibres in the uncalcified dentine or predentine shows a more or less regular pattern. I believe that some of these fibres come to a 'stop' on or near the inner border of the uncalcified dentine and develop there a 'varix' sometimes of considerable size (Fig. 1) and then, perhaps by active ingrowth, produce the nerve net mentioned above in the uncalcified dentine. This nerve net seems to have often two, three or more

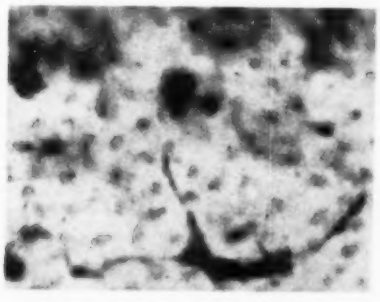

Fig. 1. Predentine, cross-section, showing a 'varix' with three nerve fibres originating from it. Left upper second premolar, girl, 14-years old, × 920

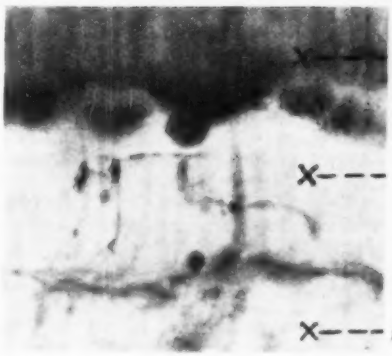

Fig. 2. Nerve fibres in the predentine running in three layers. From the same tooth as in Fig. 1. *cd*, Calcified dentine; *uncd*, uncalcified dentine; *p*, pulp; × 750

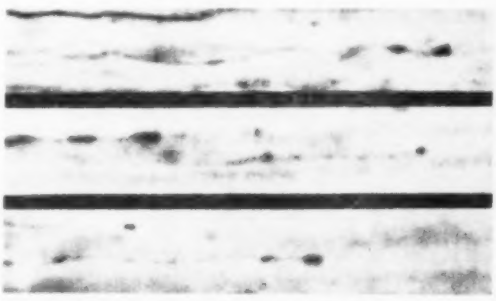

Fig. 3. Calcified dentine from a left lower second incisor of a boy 12 years old; longitudinal section. Three strips of dental tubuli with nerve fibres in it. × 1,200

layers (Fig. 2); parts of the nerve net can also be found on the lowest layer, that is, on the inner border itself. Connexions between the different layers may be very numerous and of very different kinds. Some of the nerve fibres can be followed in the dentinal tubules, where they proceed with the odontoblastic process in the distal direction. Most of the fibrils are dotted or beaded at regular intervals in the uncalcified dentine as well as in the dentinal tubules (Fig. 3), and are, as in the case of the calcified dentine, only in this way discernible because the nerve fibres themselves become very thin.

All this—and the fact that 'varices' can be found at different levels or layers—suggests, in my opinion, the following conclusion. The peripheral part of the unmyelinated nerve fibre is, at least partly, in a state of continuous regeneration, that is, development. (Peripheral regeneration of the nerves is a common experience and is known also in newly formed tissues in the region of the teeth[10] in the case of injuries but not on a physiological basis.) It may be that the functioning recipient parts of the nerve fibre are the dotted ones, in the odontoblastic area, in the uncalcified dentine and in the dentinal tubules. With the centripetal calcifying of the dentine matrix, the nerve fibre of the predentine becomes incorporated in the calcified part and ceases to function; there develops eventually from the same fibril a branch at a lower level; perhaps repeatedly. If such a fibril is exhausted, then a new one grows in the uncalcified dentine, building a varix at the termination of the pulp. The varix becomes in this way itself involved

in the developing ground substance. This explains why 'varices' can be found deep in the uncalcified dentine.

It seems highly likely that the mechanism briefly described here is not restricted to dentine, but is a regular pattern of the different subcutaneous free receptors, at least in the mucosa and in the skin.

A more detailed report of this work will be published elsewhere.

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BIOLOGY

Promotion of Cucumber Hypocotyl Growth by Two New Gibberellins

Wittwer and Bukovac[1] and Lockhart and Deal[2] have recently shown that gibberellin A_4, though less active than gibberellin A_1 or gibberellic acid in most bioassay systems[1,3,4], is far more active than A_1 or gibberellic acid in promoting the growth of cucumber stems. We have found that two recently discovered gibberellins, A_7 and A_9, both produced by *Gibberella fujikuroi*[5,6], also show specifically high activity in promotion of cucumber hypocotyl growth.

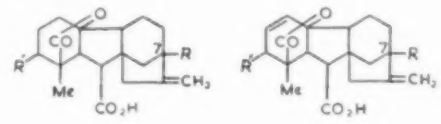
Cucumber seeds were germinated on moist filter paper at 25° C. in darkness. After 48 hr. the seed-coat was removed from germinated seeds and they were transplanted in dishes of 1 per cent water agar. The gibberellin was applied in 2-μl. drops of ethanol to the cotyledons. After 2 (Table 1) or 3 (Table 2) days growth at 25° C. in diffuse white light, the lengths of the hypocotyls were measured. The results of experiments with two varieties of cucumber, in which gibberellins A_4 and A_7 and gibberellic acid were compared, are presented in Table 1. It will be seen that both A_4 and A_7 are considerably more effective than gibberellic acid in promoting hypocotyl growth. We have found that gibberellin A_7 is of the same order of activity as gibberellic acid in promotion of lettuce hypocotyl growth, but less active than gibberellic acid in promotion of pea stem extension.

Gibberellin A_9 is much less active than gibberellic acid in promotion of pea stem or lettuce hypocotyl growth; with both plants a dose of 10 μgm. A_9 is required to give an effect comparable to that of 0·1 μgm. gibberellic acid. Nevertheless, A_9 is much more active than gibberellic acid in promotion of cucumber hypocotyl growth (Table 2). In other experiments we have confirmed the observation of Wittwer and Bukovac[1] that gibberellin A_1 is of the same order of activity as gibberellic acid on cucumbers.

Table 2. Hypocotyl Length (mm.) of Cucumber Seedlings (Means of 30 Replicates ± *S.E.*)

Dose (μgm./plant)	Long Green ridge cucumber		Perfection ridge cucumber	
	Gibberellic acid	A_9	Gibberellic acid	A_9
0·2	27·2 ± 0·9	41·3 ± 1·1	33·4 ± 0·9	42·1 ± 1·0
1·0	30·5 ± 0·8	50·9 ± 1·2	37·2 ± 1·0	51·1 ± 1·3
5·0	40·8 ± 1·0	55·8 ± 1·4	41·0 ± 1·6	53·9 ± 1·5
Untreated controls	25·3 ± 0·7		26·0 ± 0·8	

It is perhaps significant that gibberellins A_4 (I; R = H, R' = OH), A_7 (II; R = H, R' = OH) and A_9 (I; $R = R'$ = H) have one structural feature in common that distinguishes them from A_1 (I; $R = R'$ = OH) and gibberellic acid (II; $R = R'$ = OH), namely, the absence of a hydroxyl group at position 7.



(I) (II)

We hope shortly to compare these gibberellins in other bioassay systems where A_4 has been shown to have specific activity[7]. We are indebted to Dr. B. E. Cross for samples of gibberellins A_4, A_7 and A_9.

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Effect of High-Temperature Pre-Treatment on the Germination of Oil Palm Seed

It has been known for more than forty years that a high temperature is essential for the germination of oil palm seed[1], and on a commercial scale seed is germinated in sand beds exposed to the Sun, in fermentation pits or in artificially heated germinators.

Table 1. Hypocotyl Length (mm.) of Cucumber Seedlings (Means of 20 Replicates ± *S.E.*)

Dose (μgm./plant)	Long Green ridge cucumber			Perfection ridge cucumber		
	Gibberellic acid	A_4	A_7	Gibberellic acid	A_4	A_7
0·2	15·7 ± 0·6	32·0 ± 1·4	33·3 ± 1·5	15·4 ± 0·8	28·7 ± 1·2	30·4 ± 1·5
1·0	17·5 ± 1·0	32·5 ± 1·5	32·3 ± 1·7	19·5 ± 1·4	30·1 ± 1·3	35·0 ± 1·5
5·0	21·2 ± 1·1	34·7 ± 1·9	29·9 ± 1·3	18·2 ± 1·5	28·5 ± 1·4	34·5 ± 1·6
Untreated controls	16·3 ± 1·0			12·4 ± 0·7		

The optimum temperature for the germination of kernels was shown by Hussey[2] to lie between 38 and 40° C., and a temperature of 39·5° C. has been successfully adopted for germinating seed in a specially designed germinator[4].

It has also been shown[3] that an 80-day period of high temperature is sufficient for the germination of fresh seed; periods longer than this have no significant effect on the percentage germination obtained. When the seed is kept at ambient temperature (about 27° C.) after heat treatment, the rate of germination is characteristically rapid, 80 per cent germination being obtained in about 8 days, and complete germination within 15 days. If, however, the moisture content of the seed during the heat treatment is below the optimum for germination, the rate of germination at ambient temperature is lower and complete germination may take up to 6 weeks.

In a recent experiment, four 600-ml. jars covered with 0·002 in. polythene sheet and containing 50 *dura* (thick-shelled) seed were kept for 80 days at 39·5° C. at each of the four moisture contents shown in Table 1. The first of these was achieved by overwatering and maintaining a ½-in. layer of water at the bottom of the jar. In treatments 2 and 3 the seeds were examined three times a week and watered when necessary, the moisture content being estimated visually, while in treatment 4 the seeds were dried at the start of the experiment and received no water during the heat treatment. The moisture content of the seed in treatment 2 was the optimum for germination. After 80 days all jars were brought to ambient temperature. In two jars from each treatment the seeds were soaked for 5 days, then dried slightly to the optimum moisture content, and in the remaining two the seeds were left unchanged. The germination percentages obtained, together with the moisture contents determined from samples taken after the heat treatment, are shown in Table 1.

Table 1. Germination obtained from Four Batches of Seed given 80 days Heat Treatment at 39·5° C. at a Range of Constant Moisture Contents. Half the seed in Each Batch was then brought to Optimum Moisture Content for Germination and Half was left Unchanged

Seed batch	Moisture content (per cent) Nominal	Moisture content (per cent) Actual	Germination (per cent) at Original moisture content	Germination (per cent) at Optimum moisture content	Days to 50 per cent of final germination at optimum moisture content after 80 days
1	24	24·2	12	71	23·5
2	21 (optimum)	21·3	95	92	6·5
3	19	18·6	0	97	17·5
4	14	14·2	0	97	25·0

It will be seen that excellent germination may be obtained from heat-treated air-dry seed afterwards cooled at optimum moisture content, although following cooling there is a time lag before germination starts which accounts for the differences in rates of germination shown for batches 2, 3 and 4 in Table 1. In large-scale germination of seed, thrice-weekly examination of seed for watering during the heat treatment period is rendered unnecessary, and, more important, the risk of over-watering, which is more dangerous to the final germination than underwatering, is eliminated.

This high-temperature requirement of seed, a pretreatment which corresponds to the well-known low-temperature stratification of seed of temperate plants, is remarkable in that it can be satisfied at a low seed moisture content.

In a region such as Southern Nigeria with a severe 3–4 month dry season, a high-temperature requirement has an obvious survival value, ensuring germination when water becomes available for growth.

This work is continuing and will be reported in fuller detail in the Institute's Journal.

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Effect of Temperature Fluctuations on Flowering in *Salvia splendens*

In the majority of experiments that have been carried out on the interaction of day and night temperature on plant growth, a certain day temperature is selected and this is compared with varying night temperatures or vice versa. From the results of such experiments[1,2] the explanation offered for any particular combination of temperature treatments proving more favourable for the development of the plant usually rests on the hypothesis that one or more of the processes susceptible to temperature change, for example, photosynthesis, respiration or translocation, is furthered or hindered during night or day. Therefore, depending on the suitability of the temperature combination with the period of illumination, the growth of the plant is similarly furthered or hindered.

In experiments carried out in the phytotron of the University of Liège[3] using a long-day flowering variety of *Salvia splendens* Sello it was found possible to produce the same response in the growth and flowering of the plant through using combinations of day and night temperatures that were the opposite of one another.

Salvias were grown at 20 and 27° C. keeping the day and night temperature constant in both cases. Plants were also grown in long days with the temperature kept at 20° C. by day and 27° C. by night, and vice versa. The changes in temperature were controlled by thermostatic clocks, thus avoiding the necessity of moving the plants abruptly from one temperature to another. In all the temperature treatments the relative humidity was kept at 80 per cent.

Table 1 compares the growth and flowering of the plants grown in 16-hr. days under the different temperature conditions.

It is seen that there is little difference in the time taken for the plants to flower or in the height of the

Table 1. Comparison of State of Development of Salvia Plants grown in 16-hr. Days when 50 per cent of the Plants in Each Treatment (150 Plants per Treatment) have just produced their First Flowering Bud

	20° C. day and night	27° C. day and night	20° C. day and 27° C. night	27° C. day and 20° C. night
Age in days	36	38	49	53
Height (cm.)	4·6	4·6	6·3	8·6
Vegetative nodes formed	6	8	8	9

plants at flowering when the temperature is kept at 20 or 27° C. constantly day and night. However, when the temperature is allowed to vary either 20° C. by day with 27° C. by night or vice versa there is a retardation in the flowering of the plants. With both these temperature treatments the response is the same, the plants being both older and taller at flowering.

Explanations based on such hypotheses as used by Went *et al.*[1,2] are here of no avail, as opposite conditions produce in each case the same result. It can only be concluded that the alternation of temperature produces its effect without being correlated with either the period of illumination or darkness.

I am indebted to Prof. R. Bouillenne for facilities in the phytotron, to Dr. C. Sironval for advice and to the Carnegie Trust for the Universities of Scotland for a scholarship.

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Biochemical Classification of Yeasts

Roberts and Thorne[1] disagree with my proposals[2] for improving the classification of yeasts, but themselves suggest no way of overcoming the difficulties (which they acknowledge exist) in using the present system[3]. Instead, they emphasize the desirability of constructing a phylogenetic classification; though this is obviously impracticable.

I advocated developing a classification of yeasts based mainly, not, as they claim, "exclusively", on the biochemistry of yeasts. Roberts and Thorne also imply that I hold the view that because morphological differences reflect chemical ones, morphology is neither interesting nor important. This argument is a *non sequitur* and I did not put it forward.

It is strange that Roberts and Thorne object to the idea that the most important thing about yeasts is their biochemical activity. Chemical processes determine the role of yeasts in brewing, wine-making, baking, nutrition, spoiling foodstuffs and as pathogens. Thus it is not surprising that of thirteen papers on yeast genetics published by Winge and Roberts[4] between 1948 and 1958, at least nine were concerned with biochemical characteristics.

In the present lack of knowledge about the ancestral history of yeasts, it is self-deception to say that any classification of them is phylogenetic. The idea of chronology is implicit in any phylogenetic classification; and this has little meaning except in terms of the age of ancestral forms[5]. Kudriavzev's[6] and Zsolt's[7] theories of evolutionary relationships are based on insufficient evidence; and Wickerham's speculations[8] on the phylogeny of the *Hansenulae* involve false assumptions[9]. Kudriavzev held that it was necessary for his classification to be phylogenetic. Because of the difficulty in developing a phylogenetic theory for the asexual forms (p. 80), he did not publish any data on the species of non-sporing yeasts, and this detracts enormously from the value of his book[6].

The Dutch classification of yeasts[3] is by far the most complete and therefore the most useful. As I have pointed out before[2,9], it has, however, three major weaknesses. (1) Sporulation tests are given supreme importance. These involve a bewildering array of media (Phaff and Mrak[11], list 18) and extensive searching for spores. Moreover, since a negative result is equivocal, these tests are very unsatisfactory. (2) The morphological criteria used, are ill-defined and difficult to specify precisely. (3) The biochemical tests are excessively crude and hence uninformative.

Roberts and Thorne do not say that these criticisms are invalid. Assuming their validity, it seems reasonable to develop techniques for classifying yeasts in which: (*a*) there are no sporulation tests; (*b*) the morphological criteria are given greater precision; (*c*) biochemical tests are designed to give more information.

I do not suggest that studies of morphology or of sporulation should stop; but I do suggest that in classification biochemical criteria should be given more importance than at present. No embargo on evolutionary speculation has been proposed; but there is no reason why such conjecture must be applied to yeast taxonomy. Perhaps it is worth noting van Niel's striking *volte-face*: although in 1936 he held that bacterial classification had to be phylogenetic[12], ten years later he wrote: "Bacterial taxonomy is far more similar to Linnaeus's original system of the plants. . . . Both kinds of system are useful if they permit the rapid assignment of a specimen to a restricted group, but neither can lay claim to representing phylogenetic relationships", and in another passage: "It is not hereby implied that such systems are inferior to the 'natural' systems of the botanist and zoologist, but merely that they serve a different purpose, and are arbitrary"[13].

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Effects of Light and Optical Sensitization by Acridine-Orange on Living Bull Spermatozoa

Continuation of investigations on the effects of vital fluorochroming of bull spermatozoa with acridine-orange[1] has now confirmed the view that the observed adverse effects may be attributed to photodynamic action exerted by the fluorochrome.

Bull semen was diluted with optically clear egg-yolk – citrate buffer, every sample being split into

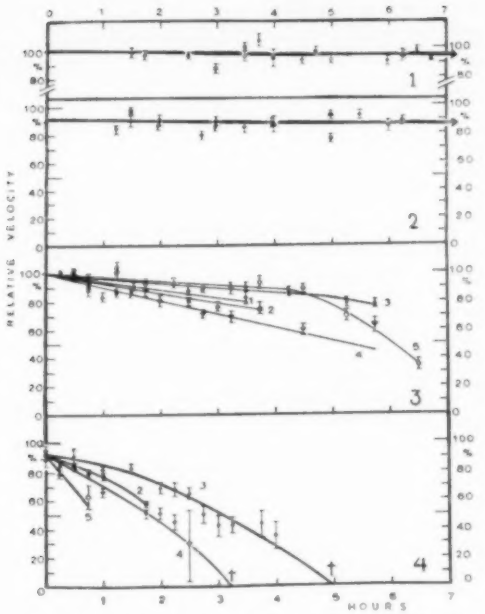

Fig. 1. Relative mean velocities of bull spermatozoa as a function of time, with and without acridine-orange.

Curve 1. Controls without acridine-orange, kept in darkness; initial mean velocities have been taken as 100 per cent; the absolute values were 107 ± 11 μ/sec. (*S.E.* ± 5).

Curve 2. Samples with acridine-orange, kept in darkness. Initial velocity 92 per cent relative to the initial mean velocity of the controls, as a result of the adverse effect of photosensitization during the measuring procedure.

The regression lines of (1) and (2) were calculated from data extending to 30 hr., only the first 7 hr. being shown here. The spread of the curves obtained in the individual experiments being very small, only the regression lines for pooled data are shown. Curve 3. Controls without acridine-orange, kept under illumination with white light. Initial mean velocity taken as 100 per cent. Curve 4. Samples with acridine-orange, kept under illumination. At † no actively swimming specimens could be observed visually under the microscope

four portions, to two of which acridine-orange in a final concentration of 1 : 50,000 was added. The darkness samples were kept in a Dewar vessel with ice, the tubes being isolated from direct contact with the ice by an air mantle. The samples used for irradiation (also isolated by an air mantle) were placed in a glass beaker with ice, separated from the light source (a 220-V., 200-W. incandescent lamp) by a cooling cylinder filled with water and ice. At regular intervals drops were taken from the test-tubes and brought into the photo-electric equipment[1–4].

With the samples kept in darkness, there was no statistical difference between the semen with acridine-orange and the control with respect to the rate of decrease of velocity, and the rate of decrease of the number of spermatozoa moving normally; however, the curves were shifted to a lower level. The amount of this constant difference per ejaculate could be accounted for completely by the effect of optical sensitization by acridine-orange during the period of measurement. The mean rates of decrease of velocity with time were 0·55 ± 0·18 (*S.E.*) μ/sec./hr. for the controls and 0·56 ± 0·17 μ/sec./hr. for the samples with acridine-orange.

In the illuminated samples the mean velocity of spermatozoa with normal movement decreased rapidly in comparison to the samples kept in darkness, the effect of addition of acridine-orange being most striking (Fig. 1). All curves bend towards the abscissa. From an analysis of much more extensive material on the rates of decrease of velocity under different conditions, it may be expected that all the curves will bend down to the abscissa if the period of taking measurements is sufficiently extended. The curves can be described by the equation:

$$\bar{v}_t = \bar{v}_0 - \alpha t.\exp(kt) \qquad (1)$$

where $\bar{v}_t$ is the mean velocity at an interval of time t after the beginning of the experiment when the mean velocity is $\bar{v}_0$; α and k are constants determining slopes and bending points. If the numerical value of kt is small, (1) reduces to the straight-line equation:

$$\bar{v}_t = \bar{v}_0 - \alpha t \qquad (2)$$

obtained in experiments of short duration relative to the rate of decrease of velocity.

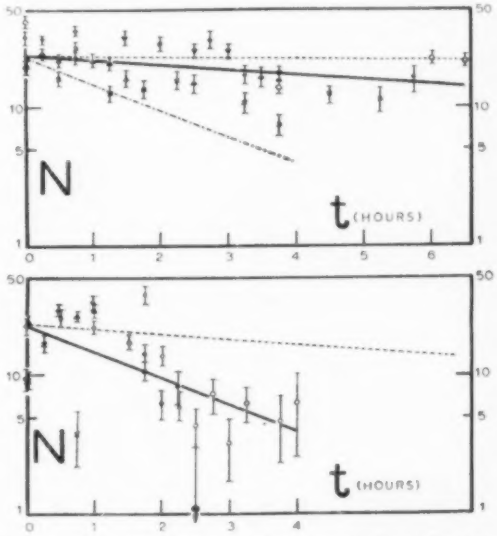

Fig. 2. Semi-logarithmic plots of numbers N per volume (in arbitrary units) of bull spermatozoa moving normally, as a function of time, under illumination with white light.
Upper graph: Controls without acridine-orange. The upper dotted line indicates the curve obtained for the samples kept in the dark, while the lower dotted line indicates the curve for samples with acridine-orange added kept under illumination. These dotted curves may facilitate comparison.
Lower graph: Samples with acridine-orange added. The dotted line indicates the curve of the illuminated control

The number N per unit volume of spermatozoa moving normally has been found to decrease exponentially with time during the limited periods actually investigated[3–6], according to:

$$N_t = N_0.\exp(-kt) \qquad (3)$$

yielding a straight-line relationship on a semi-logarithmic plot (Fig. 2). Whether this relationship would hold over an extended range is doubtful, since according to (3) the number of moving specimens would only become zero at infinite time, which is obviously impossible, the last specimen in reality becoming immotile at a very finite time indeed. With this restriction, the values of k and the half-life periods $t_{1/2}$ obtained for the four different conditions were:

Samples without fluorochrome, in the dark: $k = 0{\cdot}018$ hr.$^{-1}$, $t_{1/2} = 38$ hr.

Samples without fluorochrome, illuminated: $k = 0{\cdot}078$ hr.$^{-1}$ $t_{1/2} = 8{\cdot}8$ hr.

Samples with acridine-orange, in the dark: $k = 0{\cdot}017$ hr.$^{-1}$, $t_{1/2} = 40$ hr.

Samples with acridine-orange, illuminated: $k = 0{\cdot}43$ hr.$^{-1}$, $t_{1/2} = 1{\cdot}6$ hr.

There is no significant difference in slope between the curves obtained for the samples with and without acridine-orange kept in darkness ($P > 0{\cdot}90$). The slopes of both curves differ significantly from a horizontal line ($P < 0{\cdot}001$).

The slope of the curve of the samples without acridine-orange, kept in darkness, differs significantly from that of the illuminated portions of the same samples ($0{\cdot}02 < P < 0{\cdot}05$), illumination increasing the rate of reduction of the number of spermatozoa.

The slope of the curve of the illuminated samples with acridine-orange is significantly steeper than that of the curves obtained for the samples kept in darkness ($P < 0{\cdot}001$), and also than that of the curve obtained for the samples with acridine-orange kept in the dark.

These results confirm that the number of normally moving spermatozoa in diluted semen without the addition of fluorochrome decreases much faster under the influence of illumination than in darkness, in agreement with previous findings by Norman and Goldberg[7], whose results, however, do not allow further analysis of the relationship since evaluations were performed at two time intervals only. The ratio of the slope constants in these two conditions is obviously dependent on the actual level of illumination employed. This is not the case with a comparison between the constants for the slopes obtained for the same illuminated samples with and without acridine-orange, since both are then exposed to the same light intensity. Whereas in darkness acridine-orange (1 : 50,000) did not have any demonstrable effect on the mean velocity and the number of normally moving sperms during a period of storage in a Dewar vessel with ice up to 30 hr., a big and deleterious effect in both respects occurs in the samples kept under illumination; this effect is enhanced considerably by photosensitization by acridine-orange.

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Size of Particles ingested by *Simulium* Larvæ

The diet of the aquatic larval stages of the blackfly, *Simulium*, some adults of which transmit onchocerciasis to man and animals, has been described; but little information is available on the size of the particles ingested.

The size of particulate matter taken in by *Simulium* larvæ has been measured for four temperate species of *Simulium*.

S. ornatum was obtained from a small highly calcareous stream at Hawarden, Flintshire. This stream is heavily shaded by trees and slightly polluted by farm drainage.

S. ornatum, *S. reptans* and *S. variegatum* were collected from the River Ceirog at Chirk, Denbighshire. This river, a tributary of the Dee, is shaded by trees, is moderately calcareous, and is slightly polluted from cattle pasture.

S. tuberosum was obtained from the Hirnant, a soft-water hill stream at Bala, Merionethshire.

The contents of the midgut were separated from the gut tissue on a slide, and spread by gentle pressure on a coverslip. The longest and shortest axes of 45 randomly selected particles were measured in 5 last instar larvæ in each group, and in 5 earlier instar larvæ which were not identified, taken from the Ceirog.

The frequency distribution of particle sizes in each group was log normal, and the sizes in the individuals of the different species from the different rivers were similar.

(*S. ornatum*, Hawarden, $11{\cdot}3 \pm 1{\cdot}8\mu$, $6{\cdot}6 \pm 1{\cdot}7\mu$; *S. ornatum*, Ceirog, $13{\cdot}2 \pm 2{\cdot}1\mu$, $7{\cdot}3 \pm 1{\cdot}8\mu$; *S. reptans*, $15{\cdot}1 \pm 2{\cdot}0\mu$; $8{\cdot}0 \pm 1{\cdot}8\mu$; *S. variegatum*, $14{\cdot}8 \pm 2{\cdot}1\mu$, $7{\cdot}8 \pm 1{\cdot}9\mu$; *S. tuberosum*, $12{\cdot}0 \pm 1{\cdot}9\mu$, $7{\cdot}7 \pm 1{\cdot}9\mu$; unidentified early instars $14{\cdot}0 \pm 1{\cdot}7\mu$, $7{\cdot}3 \pm 1{\cdot}7\mu$.)

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BACTERIOLOGY

Chelating Agents for Selective Growth of Bacteria

The use of *p*H buffers for stabilizing the *p*H of growth media has become common bacteriological practice. There do not appear to be any reports, however, of the similar use of chelating agents for controlling the concentration of metal ions as 'metal buffers'[1,2]. With metal ions there is a more complex situation, of course, since there are few chelating agents selective for one particular metal. An observed effect on bacterial growth can, therefore, be due to simultaneous sequestration of several metal ions and this must be allowed for in designing experiments.

It has been found that, by suitable control of the concentration of magnesium ions, liquid and solid media can be devised for selection of coagulase-positive staphylococci in presence of coagulase-negative strains and of many commensal organisms. By calculation from the controlled *p*H and from the known stability constants of the chelating agents[3] employed, it is found that the concentration-range over which an effect can be observed in the growth-rate of coagulase-positive staphylococci lies roughly between $M/1{,}000{,}000$ and $M/25{,}000$ free magnesium ions (or if expressed more conveniently in terms of the negative logarithm, from *p*Mg 6·0 to 4·4). This accords with the value of $< M/250{,}000$ to $M/25{,}000$

found by Shooter and Wyatt[4] by returning magnesium and calcium ions to media previously exhausted by treatment with '*IRC*-50' ion-exchange resin.

A representative liquid medium which will distinguish coagulase-positive from coagulase-negative strains of staphylococci (picked from colonies on blood agar plates) after 6–24 hr. incubation at 37° C. is as follows: 'Casamino' acids (Difco), 0·2 per cent; yeast extract ('Oxoid'), 0·05 per cent; Na_2HPO_4, 0·0144 *M*; KH_2PO_4, 0·0056 *M*; Na_3H salt of ethylenediamine tetraacetic acid (Na_3HEDTA), 0·0012 *M*; Na_2 [MgEDTA], 0·006 *M*; Na_2 [CaEDTA], 0·007 *M*; Na_2[MnEDTA], 0·001 *M* (added phosphate 0·02 *M*, *p*H 7·2, calculated *p*Mg 4·8).

A representative agar medium which can be used for selection of coagulase-positive colonies in primary cultures from a slit sampler, or from sweep inocula from swabs or like sources, is as follows: Nutrient agar (Difco), 3·4 per cent; Na_2HPO_4, 0·0144 *M*; KH_2PO_4, 0·0056 *M*; Na_3HEDTA 0·00325 *M*; Na_2 [MgEDTA], 0·01 *M*; Na_2 [CaEDTA], 0·008 *M*; Na_2 [MnEDTA], 0·001 *M* (added phosphate 0·02 *M*, *p*H 7·2; calculated *p*Mg 4·6).

These recipes make allowance for the free metal ions originally present in the nutrient media used, and might require modification if different nutrients with different contents of metal ions were employed.

An early application of the agar medium has been in the detection of coagulase-positive staphylococci in pillows and mattresses (Knights, H. T., unpublished work), cultures from which are commonly overgrown by other organisms. Work on further applications of chelating agents is continuing.

I am indebted to Dr. J. D. Manning, director of the National Health Institute, who suggested work with the staphylococci originally and whose interest has been most encouraging.

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Plasma Membranes and Mitochondrial Equivalents as Functionally Co-ordinated Structures

A controversy has existed since 1951 concerning the sites of oxidative-reductive reactions in the bacterial cell. Several investigators have demonstrated biochemically the presence of oxidative-reductive systems in particulates derived from the bacterial cytoplasmic membrane and probably also from contiguous granules. Weibull[1], Mitchell and Moyle[2], Storck and Wachsman[3], Weibull and Bergström[4], Keeler, Carr and Varner[5], Cota-Robles *et al.*[6] and Weibull *et al.*[7] have presented evidence that the cytoplasmic membrane, its fragments and associated granules contain most of the cytochromes and enzymes responsible for succinate, reduced diphosphopyridine nucleotide, DL-lactate, and α-ketoglutarate oxidation and about half the L-malate oxidative activity.

Evidence of oxidative-reductive events localized in cytoplasmic granules has been advanced by Bielig, Kausche and Haardick[8], Kellenberger and Huber[9], Georgi *et al.*[10] and Mudd *et al.*[11]. A considerable literature has grown up in support of each view. The purpose of this communication is to indicate that the reality of the situation lies rather in integration than in continuing opposition of these views concerning the sites of bacterial oxidation-reduction.

In the present work strains of *Bacillus megaterium* were examined as bacterial cells, as protoplasts and as ghosts, with the light and the electron microscopes. Cell walls, septa, cytoplasmic membranes and contiguous granules were clearly visualized. Reduction of various tetrazolium salts, serving as oxidation-reduction indicators, occurred in the protoplasts very rapidly, often becoming microscopically visible immediately after addition of the indicator.

Tetrazolium salts were sometimes added to the intact bacilli in sucrose solution without lysozyme. When granules of the reduction product had become visible microscopically, lysozyme was added, thereby converting the granule-containing bacilli into granule-containing protoplasts, showing that the tetrazolium granules of the bacilli and the protoplasts were one and the same and that the granules were not associated with the cell wall. When protoplasts containing formazan granules were centrifuged and distilled water was added in place of sucrose to cause rupture of the protoplasts, the irregular, shattered membranes could be seen in wet mounts to be associated with the stained granules.

Reduction of potassium tellurite proceeded slowly in both bacilli and protoplasts and usually required several hours to produce granules; the resulting sites appeared to be similar to those produced by reduced tetrazolium salts. The protoplast membrane took on a greyish shade after long exposure to tellurite. The granules, which appear as homogeneously dark particles in the light microscope, were seen in the electron micrographs to be localized deposits of tellurium crystals.

For observation in the electron microscope cells were grown in a medium containing potassium tellurite and studied either as intact cells or as ghosts or after ultra-thin sectioning. Such preparations were fixed in buffered formaldehyde to avoid re-oxidation of the reduced tellurium by the usual fixatives. In such preparations, crystals of the reduction products were seen throughout the cells. In sections clusters of crystals were seen at sites near the periphery of the cytoplasm, and as individual crystals or amorphous grains in the periphery of the ghosts. The persistence of reduction products in the ghosts strongly suggested that the sites of reduction were in or in close association with the plasma membrane. These results are compatible with the interpretation that oxidation-reduction reactions occur both in the plasma membrane and in associated cytoplasmic organelles.

In offering a definition of bacterial mitochondria in 1956, the senior author concluded with the following sentence[11]: "There is at present no positive evidence of the existence of double membranes or *cristae mitochondriales* in bacterial mitochondria". In the intervening years electron micrographs of lamellated cytoplasmic organelles have been published by a number of authors[12–22].

The nature of the cytological association between cytoplasmic membranes and contiguous cytoplasmic organelles has most recently been defined with even greater precision in at least one genus of Eubacteria

and in Actinomycetales. In electron pictures of ultra-thin sections of *Mycobacterium tuberculosis*[24,25], of *Bacillus subtilis*[26] and of *Streptomyces coelicolor*[27] the lamellæ of the cytoplasmic membranes are seen to be continuous with the outer lamellæ of cytoplasmic organelles. In most recent work by Giesbrecht[28] on *Bacillus megaterium* 'organized' mitochondria are demonstrated the interiors of which are filled with closely packed *tubuli mitochondriales*. These mitochondria closely resemble the mitochondria of protozoa. It is greatly to be hoped that the biochemical relationships of these structures may soon be defined with equal elegance.

Preliminary accounts of this work have already appeared[29]. The work was aided by a grant from the United States Atomic Energy Commission, AEC Contract No. *AT*(30-1)-1342, and by Contract No. *E*-2690 with the Public Health Service, National Institutes of Health.

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GENETICS

Lethal Mutations in Brazilian Human Populations

A survey has been made in some socio-economically similar rural populations in three neighbouring townships in the southern region of the central State of Minas Gerais, Brazil. About 1,100 families of unskilled workers and a few small farmers were studied. These families have been classified according to the ethnic background of the spouses and grouped into six categories: White × White ($W \times W$), White × Mulatoes ($W \times M$), White × Negroes ($W \times N$), Mulatoes × Mulatoes ($M \times M$), Mulatoes × Negroes ($M \times N$), and Negroes × Negroes ($N \times N$). The Whites are almost exclusively of Portuguese ancestry. Within each class, families were grouped according to the coefficient of inbreeding f of their offspring; these values ranged as follows: 1/8, 3/32, 5/64, 9/128, 1/16, 3/64, 17/512, 1/32, 3/128, 1/64, and 0 (assumed to be non-related). A number of families where the values of f were known to be lower than 1/64, but the precise values could not be ascertained with certainty have been discarded.

In the summary presented in this communication (details will be given elsewhere), only mortality within the group with $f = 1/16$, within the total sample of consanguineous marriages, and within the outbred control will be compared (Table 1). Mortality has been divided into three categories: (1) abortions plus miscarriages (from about the second up to and including the sixth month of pregnancy); (2) stillbirths; (3) mortality from birth up to and excluding the mean age of marriage (nineteen years for women and twenty-four for men). The frequencies of abortions plus miscarriages were calculated on the basis of pregnancies (twin pregnancies being taken as one); those of stillbirths, on the basis of children born (twin births were taken as two); and mortality after birth, on the basis of live-born children. Mortality is not different among the five control samples ($x^2 = 7{\cdot}62$, for abortions plus miscarriages; $x^2 = 0{\cdot}52$, for stillbirths; $x^2 = 1{\cdot}74$, for post-birth mortality; $x^2 = 2{\cdot}80$, for the total). Among the five consanguineous samples, one value of x^2 (3·86; stillbirths) is not significant; two values (9·20 and 9·22; abortions plus miscarriages and post-birth mortality, respectively) are rather close to the 0·05 level of significance; and one value (13·88; for the total) is highly significant ($P < 0{\cdot}01$).

Mortality is generally higher in the inbred groups than in the controls, but the differences are significant only in the $M \times N$ and $N \times N$ sub-samples: abortions plus miscarriages, $M \times N$, $x^2 = 7{\cdot}97^{**}$; mortality after birth, $M \times N$, $x^2 = 11{\cdot}70^{**}$; abortions plus miscarriages, $N \times N$, $x^2 = 11{\cdot}54^{**}$; stillbirths, $N \times N$, $x^2 = 4{\cdot}12^{*}$; total, $M \times N$, $x^2 = 12{\cdot}27^{***}$; total, $N \times N$, $x^2 = 5{\cdot}84^{*}$. The higher inbreeding effect in these two classes is not due to higher mean coefficients of inbreeding (Table 1).

Within each of the five groups of marriages, the inbreeding coefficients have been pooled, when possible, to form five classes as follows: 0; 1/64; 3/128 and 1/32; 17/512 up to and including 1/16; 9/128 up to and including 1/8. In situations where some of these classes were not present or the number of observations were too small (less than 25), coefficients were pooled in a different way according to the

Table 1. Frequencies (per cent) of Mortality in the Consanguineous and Control Samples

Couples		$W \times W$	$W \times M$ plus $W \times N$*	$M \times M$	$M \times N$	$N \times N$	Total
No. of pregnancies	Control	2,375	1,137	988	357	595	5,452
	Inbred†	621	137	157	68	69	1,052
	$f = 1/16$	280	58	53	37	32	460
F_x		0·009	0·005	0·006	0·007	0·005	0·007
F_y		0·045	0·046	0·046	0·045	0·044	0·045
Abortions plus miscarriages	Control	10·40	11·52	9·41	7·28	8·74	10·07
	Inbred†	10·47	8·03	12·74	16·18	20·29	11·50
	$f = 1/16$	8·57	10·34	9·43	24·32	18·75	10·65
Stillbirths	Control	3·85	4·24	3·97	4·48	3·83	3·99
	Inbred†	4·27	7·09	4·35	5·26	9·09	5·01
	$f = 1/16$	6·59	11·54	2·08	0·00	7·69	6·28
Mortality after birth	Control	19·71	18·74	19·08	17·50	20·68	19·36
	Inbred†	18·40	22·03	19·70	35·19	24·00	20·40
	$f = 1/16$	19·09	23·91	18·75	44·83	25·00	21·91
Total‡	Control	31·12	31·31	29·86	27·17	30·59	30·61
	Inbred†	30·27	33·58	33·12	48·53	44·93	33·27
	$f = 1/16$	31·07	39·66	28·30	56·76	43·75	34·78

* The two classes have been pooled because of the small number of pregnancies in the $W \times N$ consanguineous sample.

† Total consanguineous sample, including $f = 1/16$.

‡ Calculated on the basis of pregnancies.

F_x, Mean coefficient of inbreeding of the whole sample.

F_y, Mean coefficient of inbreeding of the consanguineous fraction. In both cases, the unit has been the pregnancy.

possibilities given by their distribution. Significant positive correlation between these pooled coefficients of inbreeding and inbreeding effect was found in ($W \times M$) plus ($W \times N$), stillbirths, $r = 0{\cdot}95^*$ (d.f. = 2), and post-natal mortality, $r = 0{\cdot}90^{**}$ (d.f. = 4); in $M \times N$, abortions, $r = 0{\cdot}98^{**}$ (d.f. = 3), and post-natal mortality, $r = 0{\cdot}95^{**}$ (d.f. = 3); and in $N \times N$, abortions, $r = 0{\cdot}98^{**}$ (d.f. = 3).

Mean numbers of lethal equivalents carried by each person have been calculated according to the formula by Freire-Maia and Freire-Maia[1]. The estimates (Table 2) are suggestive of differences in the number of lethal equivalents in the two ethnic groups (Caucasians and Negroes) involved.

Negative values in Table 2 refer to situations where the frequencies of abortions (plus miscarriages) and mortality after birth were larger in the control group than in the consanguineous one. The negative total estimate for $W \times W$ ($-0{\cdot}37$) turns out to be 0·06 when one uses only the data from 1/16 up to and including 1/8, and to 0·10 with data regarding only $f = 1/16$. Morton, Crow and Muller's approach[2] leads to $-0{\cdot}18$ and Schull's variant[3] leads to 0·16 (Freire-Maia[4]).

Arbitrary values 1, 2, 3 and 4 were respectively ascribed to Whites, Light Mulatoes, Dark Mulatoes and Negroes. From these basic values, the five classes of marriages (in the order they are present in Tables 1 and 2) received the following values: 2·00, 3·35, 4·80, 6·48, and 8·00. The mean numbers of lethal equivalents estimated from the five groups of couples (that is, $-0{\cdot}37$, 1·20, 1·89, 12·15 and 9·12) are positively correlated to the above values ($r = 0{\cdot}87^*$).

Table 2. Mean Numbers of Lethal Equivalents per Person

Couples	$W \times W$	$W \times M$ plus $W \times N$	$M \times M$	$M \times N$	$N \times N$	Total
Abortions	0·03	−1·53	1·46	3·95	5·24	0·63
Stillbirths	0·18	1·26	0·16	0·36	2·39	0·45
Mortality after birth	−0·58	1·47	0·27	7·84	1·49	0·47
Total	−0·37	1·20	1·89	12·15	9·12	1·55

The method developed by Morton, Crow and Muller[2] has been applied to our $W \times W$ and $N \times N$ data, and the results, rather close to ours, revealed a significant difference at the 0·05 level between the total estimates of B for the two ethnic groups. According to a method developed by Crow[5], it was concluded that, at least among Negroes, heterotic genes seem not to contribute substantially to mortality. Their genetic load would be entirely (or almost so) of the mutational load type, that is, due to lethal and semi-lethal genes not belonging to systems of balanced polymorphism and so being maintained by recurrent mutation. This problem will be discussed in full elsewhere[4].

We want to emphasize that the results of the present work refer exclusively to the populations under investigation. No generalization can be made uncritically.

This work has been supported by grants from the Rockefeller Foundation, the National Research Council of Brazil, and the Research Council of the University of Paraná.

We thank Dr. Warwick E. Kerr and Dr. R. Vencowsky for help during the analysis of the data. We are also indebted to Dr. James V. Neel, Dr. William J. Schull and Dr. Newton E. Morton, for criticisms of a preliminary draft of this communication.

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Origin of Expressed Mutations in *Schizophyllum commune*

Previous investigations on tetrapolar sexuality in Basidiomycetes[1-3] have shown that morphologically aberrant sectors arise in surprisingly high frequency in the common-*A* heterokaryons of *Schizophyllum commune*. These heterokaryons are established whenever matings are made of two strains which share common factors at one of the two complex loci governing incompatibility, the *A* factor[1]. On further isolation these sectors are capable of growing into homokaryotic mycelia of a limited number of phenotypes, and in the majority of cases each type can be shown to be the result of a single-gene mutation[4]. No such occurrence of visibly expressed mutations has ever been observed within homokaryons. Among the hypotheses which have been proposed to account for the origin of these expressed mutations are[2]: (*a*) increased mutagenesis within the heterokaryon

at a few specific loci; (*b*) increased mutagenesis at all loci followed by selection of the few specific types encountered; (*c*) no increase in mutagenesis, but selection of a few specific types of low-level, spontaneous mutation.

The present report offers evidence which tends to support the last hypothesis. By means of a null-point method, similar to that employed by Luria and Delbrück in their classic researches on mutation in bacteria[5], the mutation-rates of three common-*A* heterokaryons and of their component homokaryons have been determined. This technique makes possible a comparison of the 'basic mutability', uncomplicated by the subsequent phenomena of nuclear migration and differential multiplication.

A number of series of replicate microcultures of each mycelial type were grown on a limiting concentration of nutrient (10^{-3} the concentration of a standard glucose–peptone medium[1]). At the end of a suitable period of growth, usually 21 days, after which time 10^6–10^7 cells were present, each microculture was individually macerated in a Waring Blendor. The fragments were plated out on complete medium, and the resulting colonies were visually screened for the presence of mutant types. On the assumption that the mutations were distributed according to Poisson's Law[5], the fraction of cultures within any one series which contain no mutants is equal to e^{-m}, where m is the average number of mutations per culture. The rate of mutation per nucleus per nuclear cycle is then equal to m divided by the average number of nuclei per culture, N. The value of N was calculated from viable fragment counts by means of a correction factor which expressed the ratio of a microscopically measured number of cells and the viable fragments surviving the maceration thereof.

It was seen, first of all, that mutations could indeed be detected in homokaryotic microcultures as well as in heterokaryons. This finding has previously been reported only sporadically[3,6]. Secondly, the rate of mutation within any one heterokaryon, about 10^{-7} per nucleus per nuclear cycle, was not appreciably higher than the rate within either of the component homokaryons. Thirdly, the various series, homokaryotic as well as heterokaryotic, showed no marked differences in the spectrum of mutations obtained; thus, fourteen more or less distinct morphological classes were isolated, and almost all classes were recoverable from any one mycelial type. Twenty-five such mutants, of various types and derived from both homokaryotic and heterokaryotic mycelia, were crossed to wild type; the mutant character segregated as a single-gene trait in every case. These experiments were repeated using 5- and 10-day-old cultures. The proportion of mutant-bearing cultures decreased in accordance with the smaller total cell population per culture, but the estimations of the mutation-rate were substantially the same as for the 21-day-old cultures. Hence, the mutation-rate appears to remain constant for at least the period 5–21 days. Although differences in expressed mutation have been observed between differently constituted heterokaryons[3], no difference in basic mutability was found between the three heterokaryons studied here. Furthermore, increasing the degree of isogenicity between the component strains of a heterokaryon (to the extent of 10 back-cross generations) had no effect on the mutation-rate or spectrum. A summary of the principal results is given in Table 1.

Table 1. Mutation-Rates computed from Various Values of m and N

Strain	Age	Mean N	m	Rate of mutation ($\times 10^{-7}$)
699	5 days	264,000	0·0516	2·0
*E*602	,,	229,000	0·0622	2·7
(699 + *E*602)	,,	762,000	0·1737	2·3
699	10 days	—	0·3852	4·2*
*E*602	,,	917,000	0·1310	1·4
(699 + *E*602)	,,	1,000,000	0·1656	1·7
699	21 days	4,055,000	0·5980	1·5
*E*602	,,	4,192,000	0·4763	1·1
447	,,	—	0·2391	0·6†
(699 + *E*602)	,,	4,030,000	0·7310	1·8
(699 + 447)	,,	6,615,000	0·4946	0·8
*B*1	,,	3,500,000	0·3293	0·9
*B*9	,,	8,858,000	0·4447	0·5
(*B*1 + *B*9)	,,	2,667,000	0·9163	3·4

* Estimated on the basis of $N = 917{,}000$.

† Estimated on the basis of $N = 4{,}112{,}000$.

To test the possibility that these results were due to the decidedly suboptimal conditions of growth obtaining within the microcultures, agar-plate mycelia of the above series were established on complete medium. Plugs from the older regions were excised, macerated, and examined for the presence of mutant fragments. It was found that mutant fragments could be recovered from homokaryons under these conditions as well. In general, mutant nuclei were present in heterokaryons in greater abundance than in homokaryons, but since there was considerable variation between individual samples of a particular mycelial type, further investigations of a more extensive nature are necessary to confirm this point.

It would appear from these preliminary results that the rate of mutation of any particular nuclear type is basically the same whether that nucleus exists (*a*) homokaryotically or (*b*) heterokaryotically in association with another nucleus having the same *A* factor. Thereafter, however, the differing mycelial conditions in homokaryons and heterokaryons operate to promote the phenotypic expression of the mutations within the latter mycelial type only. Whether the stage of subsequent mutant development which is affected is the multiplication of mutant nuclei or the phenotypic expression of existing mutant nuclei is not quite clear. The recovery of considerable numbers of mutant nuclei from homokaryons after maceration, even though the intact mycelia showed no evidence of mutant sectors, suggests that the phenotypic expression of existing mutant nuclei can in some way be suppressed or masked in the homokaryon. Experiments will be carried out shortly to determine in reconstituted systems the extent of selection against mutant nuclei in homokaryons, as well as the factors in the mycelial environment which significantly affect the degree of selection.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, January 9

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. G. H. Metson: "Recent Research in Thermionics".

ILLUMINATING ENGINEERING SOCIETY (at the Federation of British Industries, Tothill Street, London, S.W.1), at 6 p.m.—Mr. H. R. Ruff, Mr. H. E. Bellchambers and Mr. G. K. Lambert: "Modern Aids to Lighting Design—Computer Techniques".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Mr. Emil Schulthess: "Portrait of Antarctica".

Tuesday, January 10

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Scientific Papers.

INSTITUTION OF THE RUBBER INDUSTRY (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 5.30 p.m.—Mr. S. C. Stokes: "Rubber Bonded Non-Woven Fabrics"; 7 p.m.—Mr. R. L. Zapp: "Recent Developments in Butyl Rubber".

SOCIETY OF CHEMICAL INDUSTRY, PLASTICS AND POLYMER GROUP (joint meeting with the CHEMICAL ENGINEERING GROUP, at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. G. A. Rawcliffe and Dr. T. Love: "Some Industrial Uses of Plastics".

ROYAL SOCIETY OF MEDICINE, PSYCHIATRY SECTION (at 1 Wimpole Street, London, W.1), at 8 p.m.—Discussion on "Implications on Recent Genetic Research for Psychiatry". Speakers: Prof. L. S. Penrose, F.R.S. and Prof. P. Polani.

Wednesday, January 11

SOCIETY OF CHEMICAL INDUSTRY, MICROBIOLOGY GROUP (joint meeting with the SOCIETY FOR APPLIED BACTERIOLOGY, in the Barnes Hall of the Royal Society of Medicine, 1 Wimpole Street, London, W.1), at 2.15 p.m.—Meeting on "Quantitative Microbiology".

BRITISH INSTITUTION OF RADIO ENGINEERS (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6 p.m.—Annual General Meeting. 7.15 p.m.—Dr. G. F. Taylor: "Multi-layer Switching Devices".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Dr. C. B. Frisby: "Ergonomics—Fitting the Job to the Worker".

WOMEN'S ENGINEERING SOCIETY (at "Hope House", 45 Great Peter Street, Westminster, London, S.W.1), at 7 p.m.—"Ground Effect Machines". Speaker from Britten-Norman, Ltd.

Thursday, January 12

ROYAL SOCIETY OF ARTS, COMMONWEALTH SECTION (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Captain John Noel: "Photography and Exploration in the Himalayas".

INSTITUTE OF METALS, METAL PHYSICS COMMITTEE (at 17 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. J. E. Hilliard (U.S.A.): "Metallurgical Research at High Pressures".

CHEMICAL SOCIETY (in the Lecture Theatre, The Royal Institution, Albemarle Street, London, W.1), at 7.30 p.m.—Prof. R. D. Haworth, F.R.S.: "Some Problems in the Chemistry of the Gallotannins" (Pedler Lecture).

RADAR AND ELECTRONICS ASSOCIATION (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7.30 p.m.—Mr. G. Stannard: "Programme Circuits on Telephone Plant".*

Friday, January 13

UNIVERSITY OF LONDON (at Imperial College of Science and Technology, City and Guilds College, Exhibition Road, London, S.W.7), at 4.30 p.m.—Prof. C. J. D. M. Verhagen: "Education and Research into Instrumentation in the Technological University of Delft".*

Saturday, January 14

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London S.E.23), at 3.30 p.m.—Miss M. V. Thornton: "Indians of Canada".*

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT EXPERIMENTAL OFFICER (with a School Leaving Certificate with passes in three subjects at higher level, including two science subjects; a Higher National Certificate or equivalent) to be responsible for preparative work in a research programme concerned with biochemical and developmental genetics—The Secretary, Poultry Research Centre, Agricultural Research Council, King's Buildings, West Mains Road, Edinburgh 9 (January 14).

LECTURER or ASSISTANT LECTURER (Grade B) IN ELECTRONICS; and an ASSISTANT LECTURER (Grade B) IN PHYSICS—The Registrar, Welsh College of Advanced Technology, Cathays Park, Cardiff (January 14).

RESEARCH ASSISTANT (with a suitable veterinary qualification or a degree in agriculture or natural science) IN THE DEPARTMENT OF ANIMAL HUSBANDRY AND VETERINARY HYGIENE, for studies in poultry husbandry—The Secretary, Royal Veterinary College (University of London), Royal College Street, London, N.W.1 (January 14).

LECTURER (preferably with previous experience in the application of computers in statistics and/or operational research) IN THE ELECTRONIC COMPUTING LABORATORY—The Registrar, The University, Leeds 2 (January 20).

SENIOR LECTURER or LECTURER IN ELECTRICAL ENGINEERING—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee, Scotland (January 21).

SENIOR LECTURER IN GEOLOGY, and a LECTURER IN GEOLOGY at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 27).

SENIOR LECTURER (preferably with research interest in the application of mathematics to some engineering subject) in charge of the DEPARTMENT OF ENGINEERING MATHEMATICS—The Secretary, The Queen's University, Belfast, Northern Ireland (January 30).

ASSISTANT LECTURER IN PHYSICS—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (January 31).

SENIOR LECTURER (with research and teaching experience in the fields of cardiovascular physiology and respiratory physiology) IN PHYSIOLOGY at the University of New South Wales—The Agent-General for New South Wales, 56 Strand, London, W.C.2, and the Bursar, University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, marking envelope "University Appointment" (January 31).

ASSISTANT LECTURER or LECTURER IN THE DEPARTMENT OF PURE MATHEMATICS—The Registrar, The University, Liverpool (February 3).

LECTURER or ASSISTANT LECTURER (with a particular interest in sedimentary petrology) IN GEOLOGY—The Secretary and Registrar, The University, Southampton (February 3).

SENIOR LECTURER (familiar with modern methods in clinical biochemistry, and preferably holding a medical qualification) IN CLINICAL BIOCHEMISTRY at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 4).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN PHYSICS, CHEMISTRY, BIOCHEMISTRY, ENGINEERING, METALLURGY and PHARMACOLOGY or any related subjects—The Registrar, The University, Liverpool, quoting CV/N (February 11).

LECTURER or ASSISTANT LECTURER (with a good honours degree in engineering, mathematics or physics, together with suitable experience in hypersonics or noise and vibration theory) IN EITHER HYPERSONICS or NOISE AND VIBRATION THEORY IN THE DEPARTMENT OF AERONAUTICS AND ASTRONAUTICS—The Secretary and Registrar The University, Southampton (February 13).

HAZEL CLIFFORD POSTGRADUATE STUDENT, for research in medicine or in a scientific topic concerned with the advancement of medical knowledge—The Secretary to the Scholarships Committee, University of London, Senate House, London, W.C.1 (February 14).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN VARIOUS BRANCHES OF CHEMISTRY, CHEMICAL ENGINEERING, ENGINEERING, TECHNOLOGY, PHYSICS and allied subjects—The Registrar, The University, Manchester 13 (February 14).

TURNER AND NEWALL RESEARCH FELLOWS IN ENGINEERING, INORGANIC CHEMISTRY, PHYSICS and allied subjects—The Registrar, The University, Manchester 13 (February 14).

SENIOR LECTURER or LECTURER (with a higher degree, preferably a doctorate, with special qualifications in some branch of physical chemistry) IN PHYSICAL CHEMISTRY at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 15).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWS IN BIOCHEMISTRY, CHEMISTRY, ENGINEERING, PHARMACOLOGY, PHYSICS or CHEMICAL TECHNOLOGY (CHEMICAL ENGINEERING)—The Secretary, The University, Edinburgh (February 16).

LECTURER (preferably with training and/or publications in the field of human and economic geography) IN GEOGRAPHY at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 25).

LECTURER (with a Ph.D. or a degree in veterinary science with postgraduate experience in protozoology) IN PROTOZOOLOGY WITHIN THE DEPARTMENT OF PARASITOLOGY, University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, February 28).

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOW IN CHEMISTRY, BIOLOGICAL CHEMISTRY, ENGINEERING, PHARMACOLOGY, PHYSICS or in a related subject—The Registrar, The University, Bristol 8 (March 1).

DEPARTMENTAL DEMONSTRATOR IN BIOCHEMISTRY—The Administrator, Department of Biochemistry, The University, South Parks Road, Oxford (March 4).

SENIOR LECTURER (with a science degree and research experience to Ph.D. or comparable level, some experience in mineral and rock analysis and the ability to do fundamental research) IN GEOLOGY (GEOCHEMIST) at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, March 31).

ABSTRACTOR (with a sound knowledge of German and Dutch and the ability to abstract in English from these languages, Scandinavian and/or Spanish and Portuguese an added qualification, and preferably a knowledge of microbiology and/or botany)—The Director, Commonwealth Mycological Institute, Ferry Lane, Kew, Surrey.

AGRICULTURAL CHEMIST (with a good honours degree in agricultural chemistry, with some postgraduate experience, preferably in the tropics) in Sierra Leone, to advise the Director of Agriculture on specific problems, and for investigational studies in the field, including

the laying-out of field trials and their statistical analysis and interpretation—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/15/04.

Graduate Assistants (candidates wishing to proceed to the M.Sc. in mathematics) in the Department of Mathematics—Head, Department of Mathematics, Essex College, Assumption University of Windsor, Windsor, Ontario, Canada.

Graduate Assistants (candidates wishing to proceed to an M.Sc. in physics) in the Department of Physics—The Chairman, Department of Physics, Essex College, Assumption University of Windsor, Windsor, Ontario, Canada.

Reader in Applied Nuclear Physics—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

Research Fellow in Theoretical Physics, Nuclear Physics or Solid State Physics—The Secretary, Research Institute for Fundamental Physics, Kyoto University, Kyoto, Japan.

Scientific Assistant (female, preferably graduate with microbiology as one subject and an interest in virology)—The Director, Public Health Laboratory, Priorsdean Hospital, Milton Road, Portsmouth.

Scientific Officers (Mineral Dressers) (with a good honours degree in mineral dressing or mineral engineering, and preferably not over 25 years of age, with some experience in industry) in the Geological Survey Division of the Federal Ministry of Mines and Power, Nigeria, to undertake research on mineral dressing, particularly in connexion with the recovery of minerals from alluvial concentrates in the Plateau tinfields—The Appointments Secretary, Federal Public Service Commission, Nigeria House, 9 Northumberland Avenue, London, W.C.2, quoting J.2/8.

Senior Botanist (with a first- or second-class honours degree in botany or equivalent qualification and at least 15 years research experience and a good record of published work. Proven ability to plan and supervise research programmes and experience with tree crops, preferably in the tropics, is also desirable), to take charge of the Botany Division (comprising plant breeding and plant physiology sections) of the West African Cocoa Research Institute, Ghana—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.197/200/028/C1.

Senior Laboratory Technician (with a knowledge of chemistry)—The Assistant Secretary, Royal Veterinary College, Royal College Street, London, N.W.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Pure and Applied Chemistry. Vol. 1, No. 1. (The Official Journal of the International Union of Pure and Applied Chemistry.) Pp. 186. Published irregularly, four issues per volume. Subscription per volume including postage—U.K. £6; U.S.A. 18 dollars. (London: Butterworth and Co. (Publishers), Ltd., 1960.) [1210

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Bulletin of the British Museum (Natural History). Entomology. Vol. 9, No. 9: Sur les Psélaphides (Coleoptera) de l'Inde Septentrionale. Par René Jeannel. Pp. 401–456. 22*s*. Vol. 9, No. 10: On the Synonymy of some *Zygaena* Species, with Descriptions of a New Species and Subspecies from Morocco, Lep., Zygaenidae. By Hugo Reiss and W. Gerald Tremewan. Pp. 457–468+plates 22–25. 9*s*. Vol. 10, No. 1: A Taxonomic Study of the Larvae of West African Simuliidae (Diptera: Nematocera), with comments on the Morphology of the Larval Black-Fly Head. By R. W. Crosskey. Pp. 1–74. 21*s*. Historical Series. Vol. 2, No. 5: Darwin's Notebooks on Transmutation of Species. Part 4: Fourth Notebook (October 1838—10 July, 1839). Edited with an Introduction and Notes by Sir Gavin de Beer. Pp. 151–183. 15*s*. (London: British Museum (Natural History), 1960.) [1410

Chesterfield Tube Co., Ltd. Fabrication of Beryllium Tubes and Sections (a New Structural Metal with Unique Properties). Pp. 16. (Chesterfield: The Chesterfield Tube Co., Ltd., 1960.) [1410

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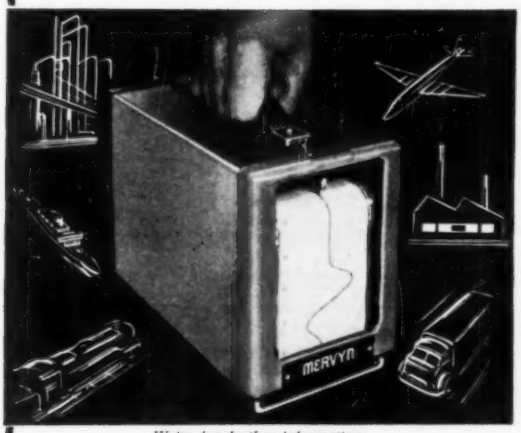

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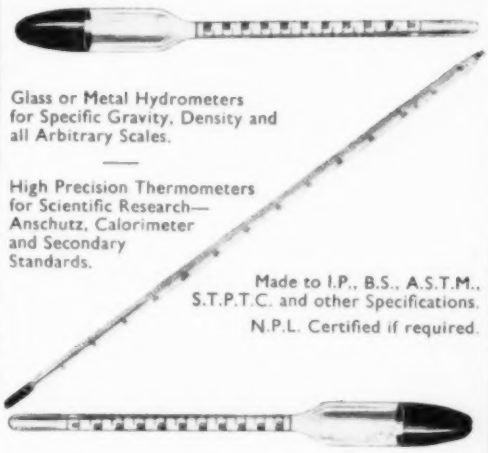

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APPOINTMENTS VACANT

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES VACANCIES FOR STAFF IN SCHOOL OF CHEMISTRY

The School of Chemistry of the University of New South Wales is under the headship of the Professor of Inorganic Chemistry (Professor D. P. Mellor) and consists of six departments. These are the Department of Organic Chemistry (Professor S. Angyal), Department of Physical Chemistry (Associate Professor R. Bosworth), Department of Inorganic Chemistry (Dr. G. Barclay), Department of Analytical Chemistry (Dr. A. Bryson), Department of Nuclear and Radiation Chemistry (Associate Professor J. Green), and the Department of Food Science and Applied Organic Chemistry (Dr. E. Cole). In addition to most of the facilities found in a modern school of chemistry, staff have access to a large electronic digital computer (an English Electric DEUCE machine, UTECOM).

The following vacancies exist:

Lecturers: (Applicants must possess a degree with honours or equivalent qualifications, and some teaching experience is desirable):

1. Two positions at Sydney. (a) Applicants for this position must have experience and/or research interests in physico-organic chemistry, particularly relating to the chemistry of foods and the colloidal properties of high polymers; (b) Applicants must have experience and/or research interests in physical chemistry, particularly in mathematical chemistry, chemical instrumentation or applied chemistry.

2. One position tenable at the Broken Hill Division (physical chemistry).

3. One position tenable at the Wollongong Division (organic or physical chemistry).

Teaching Fellows: (Applicants must possess a degree with honours in chemistry). Teaching Fellows are eligible to register for a higher degree.

Demonstrators: (Applicants must possess a degree.)

Subject to satisfactory medical examination. Lecturers will be eligible to join the superannuation scheme. Teaching Fellows and Demonstrators are subject to annual reappointment (limit for teaching fellows normally three years' service).

Salary ranges: Lecturers, £A.1,759 to £A.2,464 per annum; Teaching Fellows and Demonstrators, £A.1,129 to £A.1,349 per annum. Commencing salary according to qualifications and experience. Ship fares to Sydney paid.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, N.S.W., by airmail to arrive before February 10, 1961. Applicants outside the U.K. and Eire need only submit one copy of their application to the London address.

UNIVERSITY COLLEGE OF THE WEST INDIES

Applications are invited for: (1) Lecturer in Chemical Pathology, Department of Pathology. Duties include chemical pathological work for University College Hospital; instruction of students working for medical degrees of London University and development of new methods in a rapidly expanding teaching department. Opportunities and facilities for research excellent. Candidates should hold a degree in chemistry or biochemistry or an A.R.I.C. Experience and interest in endocrinological methods an advantage. Salary scale (under review): (medically qualified) £1,300 by £100 to £1,700 by £100 to £2,100 per annum (non-medical) £1,150 by £50 to £1,450 by £75 to £1,900 per annum. (2) Reader or Senior Lecturer in Biochemistry. The person appointed will be for the time being, Head of the recently created Department of Biochemistry. Salary scale (under review): (medically qualified) £1,600 by £100 to £2,300 per annum; (non-medical) £1,500 by £75 to £2,250 per annum (Head of Department entertainment allowance £200 per annum). Entry point determined by qualifications and experience. F.S.S.U. Child allowance. Unfurnished accommodation at rental not in excess of 10 per cent basic salary. Up to five full passages on appointment, normal termination and triennial study leave. Duties of post (two) to be assumed as soon as possible.

Detailed applications (twelve copies), naming three referees by February 6, 1961, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, from whom further particulars may be obtained.

COMMONWEALTH OF AUSTRALIA

DEPARTMENT OF SUPPLY

ELECTRO-PHYSIOLOGY

The Defence Standards Laboratories, Melbourne, Victoria, invite applications for following position of SENIOR TECHNICAL OFFICER, Grade 1.

SALARY: £1,678–£1,780 (Australian currency)

DUTIES: To provide general assistance to a small group engaged in physiological experiments to be recorded both electronically and mechanically.

QUALIFICATIONS: Applicants must have had extensive experience in physiological techniques and equipment. Knowledge of electronics desirable. Educational qualifications and experience to be stated.

CONDITIONS: This position offers permanent appointment to the Commonwealth Public Service and the successful applicant will be required to contribute to the Commonwealth Superannuation scheme on confirmation of appointment. However the appointee may alternatively choose to enter into an agreement for a three (3) year contract of employment in Australia. In this case the Commonwealth will bear the cost of return fares, together with the cost of removing the successful applicant's furniture and effects up to a maximum cost of £500 (Aust.), £250 each way. Under specified conditions, first class air/sea transport for the appointee and dependants (Wife and dependent children) will be provided by the Commonwealth.

APPLICATIONS: Forms obtainable from Senior Representative (AV.95/3), Department of Supply, Australia House, Strand, London, W.C.2, with whom completed applications should be lodged by 31st January, 1961.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH CHEMIST

The Organization's Division of Soils, Adelaide, invites applications for the position of Research Chemist at the Tasmanian Regional Laboratory, Hobart, Tasmania, from honours graduates, majoring in physical or inorganic chemistry with some years post-graduate research experience in soil chemistry, or in geochemistry or in some phase of the chemistry of micronutrients. The Tasmanian Laboratory is engaged on the study of the cobalt status of Tasmanian soils in relation to soil type, productivity and animal health. As a result of a grant from the Wool Industry Fund the programme on availability of cobalt in different soils, fixation by soils, losses by leaching and uptake by plants is to be intensified and the appointee is required to initiate, organize and actively participate in this programme. He will have the assistance of a qualified chemist and technical assistant and good laboratory and glasshouse facilities are available.

The appointment will be for an initial period of three years.

SALARY: dependent on qualifications and experience within the ranges: £A.1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid and if appointment is not extended, return fares also paid.

Further information on conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2.

to whom applications (quoting Appointment No. 273/1) should be addressed by February 11, 1961.

MIDDLESEX HOSPITAL MEDICAL SCHOOL

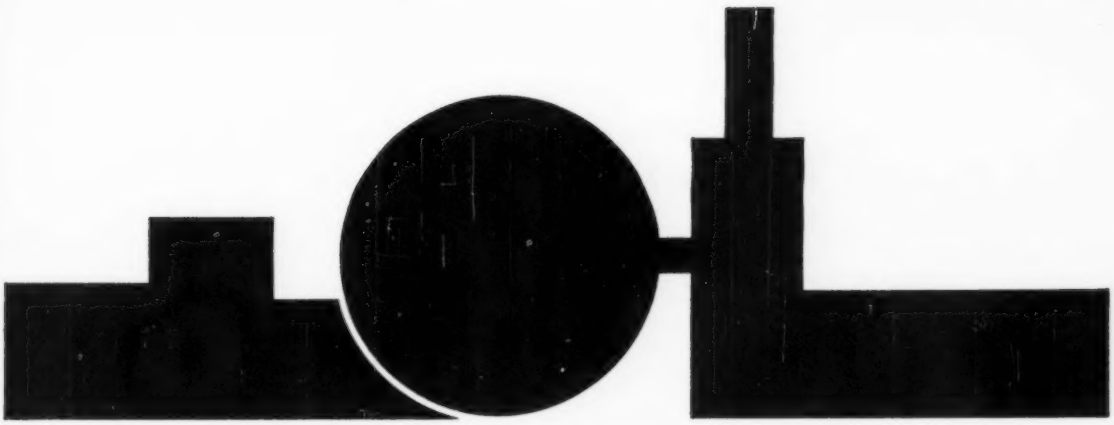
DEPARTMENT OF BIOLOGY AS APPLIED TO MEDICINE

Applications are invited for the post of Lecturer in Radiation Biology in the Department, the appointment to begin in October, 1961. The successful candidate will be expected to participate in the teaching of pre-medical, medical, and postgraduate students, but ample opportunities will be offered for research.

Applications, in triplicate, and with the names of two referees, should be made before April 1, 1961, to the Secretary, Department of Biology as Applied to Medicine, Middlesex Hospital Medical School, London, W.1, from whom further particulars can be obtained.

NATIONAL VEGETABLE RESEARCH Station, Wellesbourne, Warwick, requires Scientific Officer in Weeds Section to work on problems associated with the absorption, mobility and persistence of herbicides in soils. Qualifications: good honours degree in chemistry or botany, preferably with some postgraduate experience. Salary in scale £690 to £1,144. F.S.S.U.—Applications, with names and addresses of three referees, to Secretary by January 28, 1961.

ASSISTANT IN CANCER RESEARCH UNIT. There is a vacancy for a young research worker interested in the electron microscopic structure of cells. Starting salary £1,310.—Apply, Professor G. Causey, Department of Anatomy, Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.



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These are progressive and pensionable posts offering a real challenge and opportunity in new and expanding fields. The salary range is £755–£2,460 according to qualifications and experience.

If you have a second-class honours degree or equivalent in mathematics or physics, and, for the more senior posts, at least three years postgraduate research experience, write giving brief details to:

THE PERSONNEL MANAGER, U.K.A.E.A., DOUNREAY E.R.E., THURSO, CAITHNESS.

Please quote reference 163/34

THE CAMEROONS DEVELOPMENT CORPORATION

requires

IN ITS RESEARCH DEPARTMENT

SENIOR PLANT PATHOLOGIST

Applicants should be honours graduates in botanical subjects specializing in plant pathology with appropriate postgraduate training and should preferably have experience of one or more of the tropical crops grown by the Corporation.

PLANT BREEDER

The work will be mainly concerned with the breeding of oil palms and cocoa but selected candidate would also be concerned with the improvement of the other crops grown by the Corporation. Applicants should be honours graduates in botanical subjects, specializing in plant breeding with appropriate postgraduate training and preferably with experience of tropical crops.

These posts offer considerable scope for interesting work and for personal advancement. The Corporation has large estates in the Southern Cameroons, the main crops being oil palms, rubber, cocoa, bananas and tea. Candidates should be between the ages of 25 and 35 years. Tours will normally be of approximately eighteen months with liberal leave on full pay. Free passages are provided to and from the Cameroons for officers and their families, together with free furnished accommodation during residence in the Cameroons. A reasonable amount of free lighting and fuel is also provided, and necessary transport. An outfit allowance of £80 is payable on first appointment; children's allowances are payable up to a maximum of two at the rate of £75 each. Officers are required to contribute 10 per cent of their salary to a Provident Fund, the Corporation contributing 15 per cent.

Applicants should send full particulars to

PERSONNEL OFFICER,
COLONIAL DEVELOPMENT CORPORATION,
33 HILL STREET, LONDON, W.1.
Quoting Serial 454.

SENIOR RESEARCH OFFICER
ELECTROLYTIC ZINC COMPANY OF AUSTRALASIA LIMITED

Applications are invited for a position as a Senior Research Officer in the Company's Research Department at Risdon, near Hobart, Tasmania. Applicants should possess a university degree in chemistry or chemical engineering; they should have obtained honours or higher degrees, and should have had some years' experience in research. The Research Department is concerned with development projects and is responsible for the solution of problems which arise in connection with the Company's various activities, which include the production of zinc, ammonium sulphate, superphosphate, sulphuric acid, etc. The duties are essentially similar to those in the Research Department of any large chemical industry. Applicants should preferably be in the age range 28 to 35 years. The commencing salary offered for the position will depend on the qualifications and experience of the successful applicant, but will be at the rate of not less than £A.2,100 per annum. In addition, a bonus based on the rate of dividends declared by the Company is paid half-yearly; for 1959 the bonus was approximately 15 per cent of salary. The appointee will be eligible to participate in the Company's Staff Provident Fund and in the Medical, Hospital and Dental Schemes run by the Company. The Company will pay fares for a successful applicant and his family (if any) to travel to Australia by sea. An unfurnished house or flat can be made available on a rental basis for a married applicant.

Applications should include details of education and experience and must include details of subjects studied at the University and the standard of passes obtained. Applications should include the names of at least three referees and should be addressed to: The General Superintendent, Electrolytic Zinc Company of Australasia Limited, G.P.O. Box 377-D, Hobart, Tasmania, Australia.

UNIVERSITY OF LIVERPOOL

Applications are invited from honours graduates in science, engineering or architecture for the post of Lecturer in the Department of Building Science. The initial salary will be within the range £1,050 to £1,350 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than January 31, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Reference CV/N.

UNIVERSITY OF SYDNEY
CHAIR OF METALLURGY

Applications are invited for a recently established Chair of Metallurgy within the Faculty of Engineering. The successful applicant will be responsible for the teaching of, and research in, metallurgy and metallurgical engineering. Salary will be at the rate of £A.4,250 per annum, plus cost of living adjustments. There is retirement provision under either the Sydney University Professorial Superannuation Scheme or the New South Wales State Superannuation Scheme. Under the Staff Members' Housing Scheme, in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house. The Senate reserves the right to fill the Chair by invitation.

A statement of Conditions of Appointment and Information for Candidates may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on March 15, 1961.

D.S.I.R. ROAD RESEARCH LABORATORY, Harmondsworth, Middlesex, requires Scientific Officers or Senior Scientific Officers for research: (1) Physicists on rheology of solid-liquid systems and of viscous and visco-elastic fluids to provide basic information for design of bituminous and concrete road mixtures. (Ref. A.521/OA); (2) Chemists on problems of surface chemistry and other physico-chemical aspects of behaviour of bituminous road materials also on problems arising from presence of organic matter in soils. (Ref. F.857/OA); (3) Civil and Mechanical Engineers on (a) mechanical mixing and laying of bituminous road surfacing materials, (b) problems of design and construction of earthworks for roads (practical experience of site work an advantage), (c) stabilised soil and cement-bound base materials. (Ref. E.473/OA). Varied and interesting work both in laboratory and field, providing contacts with other scientists and engineers in U.K. and abroad. Facilities for qualifying for A.M.I.C.E. for posts (3) above. Qualifications, first- or second-class honours degree or equivalent for Scientific Officers. For Senior Scientific Officers at least three years' postgraduate experience. Salary (men) Scientific Officer, £730 to £1,205. Senior Scientific Officer, £1,330 to £1,640. Prospects of promotion in mid-thirties to Principal Scientific Officer, £1,700 to £2,375.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1 (quote appropriate reference). Closing date January 31, 1961.

UNIVERSITY OF WALES
UNIVERSITY COLLEGE OF SWANSEA
DEPARTMENT OF ENGINEERING

Owing to the large expansion of the Departmental facilities for both teaching and research, a number of appointments will be made to the Staff both immediately and from October 1, 1961. Applications are invited from graduates in Engineering, Physics, Metallurgy or Applied Mathematics for the following posts:

CIVIL ENGINEERING
Professor B. G. Neal

Lecturer or Assistant Lecturer with interests in any branch of Civil Engineering.

CIVIL OR MECHANICAL ENGINEERING

Lecturer or Assistant Lecturer with special interests in Strength of Materials and related fields.

MECHANICAL ENGINEERING
Professor R. H. Macmillan

Two Lecturers or Assistant Lecturers, one with particular interests in the fields of Heat Transfer and Thermodynamics, the other preferably having experience in the Design of Machines, but applicants with other interests will be considered.

Research Demonstrator to undertake a limited amount of teaching and pursue supervised research preferably in Heat Transfer, Hydrodynamic power transmission, Fatigue or creep.

ELECTRICAL ENGINEERING
Professor W. Fishwick

Lecturer or Assistant Lecturer with special interests in Control Engineering, Electrical Apparatus or related fields.

Lecturer or Assistant Lecturer with interests in any branch of Electrical Engineering, including Theoretical Electro-technics.

Qualifications for, and further details of, these posts are as follows: Lecturer. Applicants should hold a good honours degree and have not less than three years postgraduate experience in research or industrial design. Excellent facilities exist for research. Assistant Lecturer. Applicants should hold a good honours degree and have at least one year's industrial or postgraduate experience. Research is strongly encouraged and the assistant may register for a Ph.D. degree. Research Demonstrator. Applicants should have obtained a good honours degree and have had at least one year's industrial or postgraduate experience. The appointment will be tenable for three years, during which time the holder will be expected to work for the Ph.D. degree, submitting a thesis at the end of the period.

Salaries are on the following scales, to which are added F.S.S.U. benefits and family allowances. Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 per annum; Assistant Lecturer, £800 by £50 to £950 per annum; Research Demonstrator, £700 per annum.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (two copies), must be received not later than Saturday, January 21, 1961.

UNIVERSITY OF DURHAM
CHAIR OF PHYSICS

Applications are invited for a Chair of Physics tenable in the Newcastle Division. This is a newly established post and will be the third Chair of Physics in the Department at Newcastle. The successful candidate will be required to take up duty on August 1, 1961, or such earlier date as may be arranged. Salary in accordance with the Professorial scale (£2,600 to £3,000) with family allowance and membership of F.S.S.U.

Further particulars may be obtained from the undersigned with whom applications (twelve copies), must be lodged not later than February 18, 1961. (Candidates outside the British Isles may submit one copy only.)

E. M. BETTENSON, Esq.,
Registrar.

University Office,
46 North Bailey, Durham.

METROPOLITAN BOROUGH OF ST. MARYLEBONE
MEDICAL LIBRARIAN—PUBLIC LIBRARIES

Applications are invited for a new appointment as Librarian-in-Charge of the Special Medical Collection (Metropolitan Boroughs Special Collections Scheme). Salary in accordance with Grade APT.II, minimum £840 per annum (£855 if aged 26 or over), rising to £1,000 per annum. Candidates must be Chartered Librarians with suitable experience. Permanent superannuable appointment.

Application form and further details of appointment from Establishment Officer, Town Hall, St. Marylebone, W.1. Completed applications must be returned by noon on Monday, February 20, 1961.

THE UNITED KINGDOM ATOMIC ENERGY AUTHORITY

requires

TECHNICAL RECORDS OFFICERS

AT WINDSCALE AND CALDER WORKS, CUMBERLAND

The Technical Records Department provides a comprehensive service to management covering technical and economic aspects of the operation of nuclear reactors and chemical plants processing nuclear fuels.

Initially successful applicants will be responsible to a more senior officer for, either the Calder Works Technical Records Office which has been operating for some years, or for the Advanced Gas Cooled Reactor Office which will commence operation in the near future. A considerable variety of work is covered by these posts ranging from the accounting for process materials and the preparation of graphical and tabular data for management, to the preparation of technical budgets.

These posts would be suitable for persons who wish to obtain a sound basic knowledge of the operation of Nuclear Reactors and their associated power plant. Promotion prospects are good and selected candidates will be given opportunities to move around within the Technical Records Department, thus allowing them to obtain experience in all phases of the work.

A pass degree or H.N.C., in an appropriate subject is normally expected. All applicants should have experience of work in this field, but those with less than the normal qualifications will be required to have had exceptionally good experience.

Salary within the scale £1,110 (at age 26) to £1,360 per annum.

Contributory superannuation. Staff Housing Scheme.

Send for application form, preferably by postcard, quoting reference P/W81/J14 to: Staff Appointments Officer, U.K.A.E.A., Production Group, Windscale and Calder Works, Sellafield, Seascale, Cumberland.

Closing date January 22, 1961.

INTERNATIONAL COMPANY

with wide interests in animal products has the following vacancies in new research and development laboratories in Central London:

Pharmacology:	Head of Department.
Analysis:	Deputy Head.
Oils and Fat Products:	Deputy Head.

There are also the following vacancies for qualified and junior staff with experience in **one** or **more** of the appropriate fields:

Analysis:	Foods or allied products.
Meat Technology:	Manufactured products; frozen foods.
Biochemistry:	Proteins; steroids; enzymes.
Cosmetics:	Emulsions; perfumery; soaps.
Glyceride Fats:	Refining; hydrogenation; margarine.
Bacteriology:	Factory hygiene; foods; industrial microbiology.
Organic Chemistry:	Proteins; steroids; fine chemicals.

Apply in writing, stating age, qualifications and experience, to Box No. 939, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

UNIVERSITY OF OXFORD

It is proposed to appoint a Demonstrator in Inorganic Chemistry from October 1, 1961. The initial salary will be not less than £900 (plus children's allowances) and the post may be held in conjunction with a College Fellowship.

Applications with academic record, statement of research interests and names of two referees, should be sent to Dr. Lee's Professor of Chemistry, Physical Chemistry Laboratory, South Parks Road, Oxford, not later than March 1, 1961.

ST. EDMUND HALL, OXFORD

OFFICIAL FELLOWSHIP IN INORGANIC CHEMISTRY

The Governing Body proposes to appoint an Official Fellow in Inorganic Chemistry from October 1, 1961. The post may be held in conjunction with a university post. A demonstratorship in Inorganic Chemistry is advertised by the Inorganic Chemistry Laboratory from the same date.

Applications, with a brief statement of academic record and research interests, should be sent, not later than March 1, 1961, to the Principal, St. Edmund Hall, Oxford, from whom further details may be obtained.

ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY

GLASGOW

Applications are invited for a new Senior Lectureship in Mathematics. Preference will be given to a candidate active in magneto-fluid dynamics or plasma physics and able to initiate research in one of these fields. The salary scale is £1,975 by £75 to £2,275. Superannuation is through the F.S.S.U. and children's allowances are paid.

Applications should be lodged with the Secretary of the College, George Street, C.1 (from whom further details may be obtained), not later than January 31, 1961.

McINDOE MEMORIAL RESEARCH UNIT

QUEEN VICTORIA HOSPITAL, EAST GRINSTEAD

Applications are invited for the full-time post of Johnson and Johnson Research Fellow, to investigate problems of Tissue Transplantation. The successful candidate should have previous experience in this or related fields. Facilities will be available for any method of approach to this problem whether along immunological, biochemical, cytological or clinical lines. Salary within the range of £1,650 to £2,000, entry point dependent on qualifications and experience, annual increment £100, but a higher salary scale would be considered for a senior applicant. Tenure three years in first instance.

Further particulars available from the Secretary, East Grinstead Research Trust, Queen Victoria Hospital, East Grinstead, with whom applications should be lodged, together with the names of three referees, not later than February 24, 1961.

JAMAICA COLLEGE OF ARTS, SCIENCE AND TECHNOLOGY

KINGSTON

Principal: H. Falkner, M.Sc.(Wales), B.Sc.(Lond.), A.Inst.P.

Applications are invited for appointment as Head of the Department of Science. Salary scale: £1,750 by £50 to £2,000. Entry point according to qualifications and experience. Appointment may be either permanent or on contract. Possible housing assistance. The College is a rapidly developing one.

Further information obtainable from Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2, to whom applications (six copies), giving age, qualifications, experience and names of three referees should be sent by January 31, 1961.

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES VACANCIES FOR STAFF IN SCHOOL OF APPLIED PSYCHOLOGY

The School of Applied Psychology of the University of New South Wales consists of an academic staff of sixteen under the headship of the Professor of Applied Psychology, Professor J. F. Clark. The undergraduate work of the School consists in the preparation of students taking psychology (applied and pure) both at pass and honours levels in the Faculties of Arts, Science and Commerce. In addition psychology is taught to students in the Faculties of Medicine, Applied Science and Engineering. The School also prepares candidates for the Masters' Degree and for the Doctorate of Philosophy. The general work of the School is partly in the applied fields, e.g., industrial, counselling, clinical, and partly in pure psychology. A variety of research programmes in both pure and applied fields are in operation, and research facilities are available to staff. Lecturers are expected to assist generally in the work of the more elementary classes, and for this reason a sound basis in general psychological theory is essential. However the size of the School now enables reasonable opportunities for staff to work in their own field of specialization. Applicants with research and specialized experience in the following fields are specially sought: General, Experimental, Statistics and Psychometrics, Clinical and Applied Psychology (particularly industrial).

The following vacancies exist: Lecturer, Teaching Fellow, Senior Tutor.

Applicants should possess the following academic qualifications: Lecturer. A degree with honours in psychology or equivalent qualifications, and some postgraduate experience in research. Teaching Fellow. A degree with honours in psychology. Senior Tutor. A degree, preferably with teaching experience.

Further details may be obtained from the Head of the School of Applied Psychology, Kensington. Subject to satisfactory medical examination, lecturers will be eligible to join the superannuation scheme. Teaching fellows and senior tutors are subject to annual reappointment (normal maximum tenure for teaching fellows being three years).

Salary ranges: Lecturer, £A.1,759 to £A.2,464 per annum. Senior Tutor, £A.1,759 to £A.2,074 per annum. Teaching Fellow, £A.1,129 to £A.1,349 per annum. Ship fares to Sydney paid.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded by airmail to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, N.S.W., to arrive before February 10, 1961. Applicants outside the U.K. and Eire need only submit one copy of their application to the London address.

D.S.I.R., ROAD RESEARCH LABORATORY, Harmondsworth, Middlesex, requires Scientific Officers or Senior Scientific Officers (1) (Physicist) to develop methods of determining the density, moisture content or bitumen content of road-making materials in situ by techniques involving the absorption or back-scattering of gamma radiation and neutrons. Familiarity with electronic apparatus employed in measuring intensity of radiation an advantage. (2) Civil Engineer or Physicist to study the ability of layers forming a road to spread the dynamic loads applied by the wheels of moving vehicles. The field work on this project involves measuring the transient stresses and strains in various forms of road construction. Sufficient mathematical ability for analysis of distribution of stress and strain in multi-layer elastic structures an advantage. Qualifications: first- or second-class honours degree in physics, civil engineering or equivalent. For Senior Scientific Officer at least three years' postgraduate experience. Salary ranges: (men), Scientific Officer, £730 to £1,205. Senior Scientific Officer, £1,330 to £1,640. Normal prospects of promotion in mid-thirties to Principal Scientific Officer (£1,700 to £2,375).—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.5277/OA. Closing date January 24, 1961.

NATIONAL VEGETABLE RESEARCH Station, Wellesbourne, Warwick, requires Scientific Officer or Senior Scientific Officer to work on biochemical processes in seeds and seedlings. Qualifications: Good honours degree, preferably with postgraduate experience. Salary: Scientific Officer (£690 to £1,144), or Senior Scientific Officer (£1,250 to £1,540). Contributory superannuation scheme.—Applications, with names and addresses of three referees, to Secretary by January 21, 1961.

THE MIDLANDS RESEARCH STATION OF THE GAS COUNCIL

PILOT PLANT OPERATORS

The Station, which is at Solihull, Warwickshire, is developing, on the large pilot plant scale, new high pressure processes for town gas production by the gasification and hydrogenation of coal and oil. It invites applications from men who will take a responsible part in the control and operation of these plants under the supervision of the research scientists in charge. A qualification of least of Higher National Certificate level in Chemistry or Chemical or Mechanical Engineering will be an advantage. Shift work is involved.

The salary will be within the range of £830 to £930 per annum.

Apply, in writing, to the
Industrial Relations Officer,
West Midlands Gas Board,
6 Augustus Road, Edgbaston,
Birmingham, 15.

UNIVERSITY OF DURHAM
SECOND CHAIR OF GEOLOGY

Applications are invited for a Chair of Geology tenable in the Newcastle Division of the University. This is a newly established post and will be the second Chair of Geology in the Department at Newcastle. The successful candidate will be required to take up duty on August 1, 1961, or such other date as may be arranged. Salary in accordance with the Professorial scale (£2,600 to £3,000 a year) with family allowance and membership of F.S.S.U.

Further particulars may be obtained from the undersigned with whom applications (twelve copies), must be lodged not later than February 11, 1961. (Candidates outside the British Isles may submit one copy only.)

Registrar

University Office,
46 North Bailey, Durham.

UNIVERSITY OF DURHAM
CHAIR OF APPLIED MECHANICS

Applications are invited for a Chair of Applied Mechanics, tenable in the Newcastle Division. This is a newly established post and will be the third Chair in the Department of Mechanical Engineering at Newcastle. The successful candidate will be required to take up duty on August 1, 1961, or such other date as may be arranged. Salary in accordance with the Professorial scale (£2,600 to £3,000 a year) with family allowance and membership of F.S.S.U.

Further particulars may be obtained from the undersigned with whom applications (twelve copies), must be lodged not later than February 18, 1961. (Candidates outside the British Isles may submit one copy only.)

Registrar.

University Office,
46 North Bailey, Durham.

McMASTER UNIVERSITY
POST-DOCTORAL FELLOWSHIPS IN PHYSICS

Applications are invited for National Research Council and other Post-Doctoral Fellowships, tenable in the Department of Physics, McMaster University. Successful applicants may choose to work full-time on their research or to supplement their research with a modest amount of lecturing.

Inquiries and applications should be addressed to Professor H. E. Duckworth, Chairman, Department of Physics, McMaster University, Hamilton, Ontario, Canada.

THE MEDICAL RESEARCH COUNCIL requires a Cytologist or Trainee Cytologist at its Population Genetics Research Unit, Old Road, Headington, Oxford. The work would be concerned with a considerable variety of human cytology. Applicants would preferably, but not necessarily, have had previous experience of this type of work but should be qualified in zoology or medicine. The starting salary offered depends on qualifications and experience and could range from £700 to £1,500. Superannuation.—Applications, giving full details, should reach the Director at the above address by January 31, 1961.

SIERRA LEONE
AGRICULTURAL CHEMIST

To advise the Director of Agriculture on specific problems and for investigational studies in the field including the laying out of field trails and their statistical analysis and interpretation. Candidates (male) must have a good honours degree in agricultural chemistry with some postgraduate experience preferably in the tropics. Appointment is on contract/gratuity terms for two tours of service in the first instance with emoluments in scale £1,039 to £1,924 per annum. Gratuity 15 per cent of aggregate emoluments. Free passages on appointment and leave for officer, wife and up to three dependent children under eighteen years of age. Children's allowances. Furnished accommodation, generally available, at moderate rental. Generous leave.

Apply, stating name in full and giving brief details of qualifications and experience, to Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/15/04/C1.

LEVINGTON RESEARCH STATION
FUNDAMENTAL RESEARCH

A RESEARCH SCIENTIST is required, trained in classical physics, applied mathematics, fluid dynamics, physical or theoretical chemistry or in an engineering science, with research experience and preferably a research degree. The work, loosely described as "fundamental chemical engineering research," will involve theoretical and experimental investigations of processing operations such as transfer of heat, mass, simultaneous heat and mass, and chemical potential to collections of discrete solids and drops; physical action of solid upon solid; fluid mechanics of fluid-solid systems; transient behaviour of well defined flow-systems and of processing plant; and other problems. Experience in one of these is desirable but research training and aptitude, an analytical approach to problems, and fairly high mathematical ability are essential.

The work is a Bramford Development Station (near Ipswich), a physically separate part of Levington Research Station. Pilot plants at Bramford provide continuity between investigations of fundamental, microscopic, concepts and the industrial complex of processes. A laboratory, into which the scientist can incorporate his ideas, is to be furnished, and a library is arising. Additional facilities are available at Levington—library, X-ray and other forms of analysis, electron microscope, and specialized advice on statistical, chemical and physical analysis. Staff are encouraged to publish.

Salary according to experience and qualifications.

The Company operates a Pension Scheme which, for married staff, includes provision for widows and dependent children.

Applications, with full particulars, to Personnel Manager (KN10), Fisons Fertilizers Limited, Harvest House, Felixstowe, Suffolk.

UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND

Applications are invited for: (1) Two Fellowships in Arthropod Physiology. Tenure three years. Appointment in scales A and B below. Candidates should have a good first degree in zoology, and for appointment to the higher scale, substantial research experience. (2) Three Fellowships in Snail Ecology, for work on the ecology and physiology of the snail vectors of schistosomiasis. Appointments normally in scale C. Tenure five years, and mid-term return passages for appointee also paid. Salary scales: (A) Junior Research Fellow, £750 by £50 to £1,000 per annum. (B) Research Fellow, £1,200 by £50 to £1,400 per annum. (C) Senior Research Fellow (i) £1,500 by £50 to £1,700 per annum, (ii) £1,800 by £50 to £2,000 per annum. Superannuation and medical aid schemes. Return passages to Salisbury for appointee. Housing allowance of £100 per annum if unfurnished college accommodation at 15 per cent of salary is not provided.

Detailed applications (six copies), naming three referees, by January 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

CENTRAL ELECTRICITY GENERATING BOARD
EASTERN DIVISION

Applications are invited for the following appointment:

MATHEMATICAL ASSISTANT—BRADWELL (NUCLEAR) GENERATING STATION (ESSEX)

Salary range £670 to £805 per annum.

The commencing salary will depend upon age and qualifications.

Applicants should be young mathematics graduates.

The work will be varied in nature, involving analysis and calculations based on physical measurements made on the nuclear reactors, in order to ensure their safe and efficient operation.

Opportunities to write programmes for a large, modern computor (I.B.M. 709) will arise, and a period of training for this type of work will be provided.

Applications, quoting Reference No. S.V.1417, stating age, details of education, experience and present position, should be sent to the Controller, Central Electricity Generating Board, Eastern Division, West Farm Place, Chalk Lane, Cockfosters, Barnet, Herts, by January 14, 1961.

AUSTRALIA
THE UNIVERSITY OF NEW SOUTH WALES SENIOR LECTURER IN MEDICAL PHYSICS FACULTY OF MEDICINE

The University invites applications for appointment to the position of Senior Lecturer in Medical Physics in the School of Physiology within the Faculty of Medicine. Salary: £A.2,579 range £A.3,029 per annum. Commencing salary according to qualifications and experience. Applicants should be graduates in physics or electrical engineering with experience in the application of electronics to modern research problems. Duties will include the establishment of the School's electronic laboratory and workshop and participation in the teaching programme for science and medical students. The School's research activities lie primarily in the fields of cardiopulmonary physiology and neurophysiology and the successful applicant will be expected to participate in these activities; previous experience in physiology is not essential. First-class ship fares to Sydney of the appointee and his family will be paid. Appointee will be eligible, subject to satisfactory medical report, to contribute to the State Superannuation Fund.

Four copies of applications (including the names of two referees) should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, N.S.W., by airmail to arrive before February 10, 1961. Applicants outside the United Kingdom and Eire need only submit one copy of their application to the London address.

HILL FARMING RESEARCH ORGANIZATION

Applications are invited from honours graduates (or those expecting to graduate with honours in 1961) in botany, agricultural botany or plant Husbandry for a vacancy which will shortly arise in the grade of Scientific Officer on the Organization's Botany Staff at the hill research farm of Sourhope, near Kelso, Roxburghshire. Salary scale £690 to £1,144 per annum. Superannuation under F.S.S.U.

Further particulars and application form may be obtained from the Secretary, Hill Farming Research Organization, 48 Palmerston Place, Edinburgh 12. The closing date for applications will be January 28, 1961.

WOOL INDUSTRIES RESEARCH ASSOCIATION

A vacancy occurs for a Mathematician with special interest in applied mathematics or theoretical physics, lively mind, and interest in investigating wide variety of problems (mechanical, physical, numerical, etc., in nature) arising in textile research. Ph.D. or previous research experience desirable. Starting salary up to £1,590 per annum (with F.S.S.U. benefits), according to qualifications and experience.

Apply to the Association, Torridon, Headingley Lane, Leeds, 6.

CIBA (A.R.L.) LIMITED

have a vacancy for

A CHEMIST FOR WORK ON ADHESIVES

Candidates should be aged under 30 and must have an Honours degree in Chemistry. They should also have at least three years' experience in a position where fundamental knowledge has been applied to practical applications. This experience need not necessarily have been in the adhesives field, but preference will be given to candidates with experience of synthetic resins.

The work will consist of the formulation of synthetic resin adhesives to solve a variety of bonding problems.

Working conditions are excellent, staff benefits and salaries comparing very favourably with other companies. The factory is located in a pleasant country village eight miles outside Cambridge.

Applicants should write to the Assistant Secretary, CIBA (A.R.L.) Limited, Duxford, Cambridge, setting out full details and stating their present salary.

ENGLISH ELECTRIC VALVE CO. LTD.

CHELMSFORD, ESSEX

A PHYSICIST or MATHEMATICIAN

is required for research on electron optical systems.

Applicants should possess a first or second class honours degree in physics or mathematics and be preferably within age range 22 to 30.

Salary will take into account age and any previous relevant experience.

Apply to Dept. G.P.S., English Electric House, Strand, London, W.C.2, quoting reference N.1595L.

SYNTHETIC AND PHYSICAL ORGANIC CHEMISTS

ICI

SYNTHETIC AND PHYSICAL ORGANIC CHEMISTS

are required by

PLANT PROTECTION LIMITED

(a subsidiary of IMPERIAL CHEMICAL INDUSTRIES)

at its Research and Development Station

at JEALOTT'S HILL, near BRACKNELL, BERKSHIRE

for work on biologically active chemicals for use in crop protection. Applicants should possess good honours degrees in chemistry and post-graduate experience either at a university or in industry. They should not exceed 30 years of age and should write in the first instance, giving brief particulars only, to the Staff Officer, Plant Protection Limited, Fernhurst, near Haslemere, Surrey

HER BRITANNIC MAJESTY'S
CIVIL SERVICE COMMISSION
and
THE UNITED KINGDOM
ATOMIC ENERGY AUTHORITY
will be holding joint
Selection Boards
in
Several Centres
throughout the United States of America
beginning
MARCH 27, 1961
to interview candidates for
SENIOR and JUNIOR FELLOWSHIPS
and for
PERMANENT APPOINTMENTS
in the
SENIOR SCIENTIFIC OFFICER
and
SCIENTIFIC OFFICER GRADES

in British Government Research and Development Establishments and in the Establishments of the United Kingdom Atomic Energy Authority.

British scientists resident in the United States of America are invited to apply for further details to:

THE DIRECTOR,
UNITED KINGDOM SCIENTIFIC MISSION,
1907 K STREET N.W.,
WASHINGTON, 6, D.C.

The closing date for receipt of applications in Washington will be:

FEBRUARY 1, 1961.

OLDCHURCH HOSPITAL ROMFORD, ESSEX

(709 Beds)

RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

ELECTRONICS MECHANIC WITH LIGHT fitting and turning experience required to build and maintain electronic and instrumentation devices for agricultural engineering research and assist experimental work. Time served or ex-Service tradesman would suit. City and Guilds Certificates or National Certificate desirable. Superannuated staff post. Grade Senior Assistant (Scientific). Minimum age 25. Salary £755 to £1,010.—Further particulars from Secretary, N.I.A.E., Scottish Station, Howden, Mid Calder, Midlothian.

UNIVERSITY OF BIRMINGHAM

FACULTY OF ARTS

SECOND CHAIR WITHIN THE DEPARTMENT OF THEOLOGY

The University intends to fill a newly established second Chair within the Department of Theology. For this purpose, the University is seeking a scholar whose interests stretch across the boundaries between theology, the natural sciences and philosophy to develop work in this general area. The new Chair, provided by the Edward Cadbury Trust, has been established for seven years in the first instance. At this stage, the University would be glad to hear of and from those who are suitably qualified, and whose interests are of the kind mentioned.

Letters should be addressed to the Registrar, Dr. G. Templeman, the University, Birmingham, 15, as soon as possible, and, in any case, before March 1, 1961.

NATIONAL VEGETABLE RESEARCH Station, Wellesbourne, Warwick, requires Officer to assist in field experimental work. Degree in science, or diploma in horticulture or agriculture. Salary (Assistant Experimental Officer grade) in scale rising to £920 per annum. Contributory superannuation scheme.—Further particulars from Secretary.

BRISTOL COLLEGE OF SCIENCE AND TECHNOLOGY

ASHLEY DOWN, BRISTOL, 7

The Governors invite applications for the post of Assistant, Grade B, in the Department of Physics. Applicants should possess an honours degree in physics and have had research or industrial experience in some branch of Applied Physics. Teaching experience desirable. Salary, according to experience and qualifications, within the range £790 to £1,435.

Application forms and details from the Registrar.

UNIVERSITY OF DURHAM

Applications are invited for the newly established Chair of Inorganic Chemistry tenable in the Newcastle Division of the University. The successful candidate will be required to take up duty on August 1, 1961, or such other date as may be arranged. Salary in accordance with the Professorial scale (£2,600 to £3,000 a year) with family allowance and membership of F.S.S.U.

Further particulars may be obtained from the undersigned with whom applications (twelve copies) must be lodged not later than February 25, 1961. (Candidates outside the British Isles may submit one copy only).

REGISTRAR,
University Office.

46 North Bailey,
Durham.

NATIONAL INSTITUTE OF AGRICULTURAL BOTANY

Applications are invited for the following posts: (1) Technical Officer (Horticultural Crops). Candidates should be graduates in horticulture, or in botany with horticultural experience. Starting salary for men, £965 at age 25 or over; maximum of scale £1,510. (2) Assistant Trials Officer at Leeds University Farm, Headley Hall, Yorks. Practical experience in crop production an advantage. Starting salary for men with good honours degree £690, and for others £670, maximum of scale £930; some allowance can be made for postgraduate training. Promotion prospects. Posts (1) and (2) Superannuation under F.S.S.U. (3) Technical Officers holding degrees in agriculture or agricultural botany (a) to assist in work on Herbage Seed Production, (b) for Cereals Section, Trials Branch. Starting salary for men and women, £560 at age 21, rising to a maximum of £1,240. Superannuation Scheme.

Further particulars and application forms from M. G. Tozer, Secretary, N.I.A.B., Huntingdon Road, Cambridge.

APPLICATIONS ARE INVITED FOR THE post of Director of Jute Research (Technology) at a newly established Jute Research Institute near Dacca, East Pakistan. Will be required to take charge of technological research on jute and to advise the Central and Provincial Governments on matters relating to technological research on jute and others fibres. Should be preferably a physicist with experience of research in fibre technology at a Textile Research Institute in this country. Salary £3,500 per annum (subject to U.K. income tax) plus tax-free overseas allowance of £1,320 per annum (married) or £725 per annum (single) and other allowances. Furnished accommodation for married man provided. Duration three years in the first instance. Contract with U.K. Government.—For further information and application form write Ministry of Labour (E.9), Almack House, King Street, London, S.W.1, quoting A12/PAK/163/TCS.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

RESEARCH IN RHEOLOGY

Applications are invited from physicists for a position as experimental Research Assistant in the Department of Mathematics to continue and develop a fundamental investigation of the rheological properties of concentrated polymer solutions. Recently developed apparatus is available for the measurement of flow birefringence and normal and shear stress components in shear flow. The work calls for initiative in the design and construction of new apparatus, and for the ability to perform series of observations of sustained accuracy. Candidates should possess a good honours degree in physics. The position is tenable for two years in the first instance. Salary will be £675 per annum, and the post will be superannuable under F.S.S.U.

Applications should be forwarded to the Registrar, the Manchester College of Science and Technology, Sackville Street, Manchester, 1, on or before January 31, 1961.

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF AERONAUTICS AND ASTRONAUTICS

Applications are invited for the post of Lecturer or Assistant Lecturer in either hypersonics or noise and vibration theory. Candidates should have a good honours degree in engineering, mathematics or physics together with suitable experience in hypersonics or noise and vibration theory. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475. Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton, to whom applications (seven copies from United Kingdom applicants) should be sent not later than February 13, 1961.

NATIONAL PHYSICAL LABORATORY, Teddington, Middlesex, requires officers to work in field of neutron physics. 1. In Scientific Officer Class (Ref. A.535/OA), both physicists and chemists are required to initiate and assist in neutron cross-section measurements, precision measurements of nuclear level schemes and construction of semi-conductor detectors for nuclear radiations. Also in field of crystal diffraction as applied to neutron and gamma-ray spectroscopy. Qualifications: first- or second-class honours degree in physics or chemistry, or equivalent. Salary: Scientific Officer, £730 to £1,205; Senior Scientific Officer, £1,330 to £1,640 (at least three years' postgraduate research experience required). 2. Experimental Officers (Ref. A.536/OA) are required to work with Scientific Officers on duties set out above. Qualifications: Pass degree, H.N.C. in Applied Physics or Chemistry, or equivalent. Age not below 26. Salary: £1,075 to £1,325.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference.

DEPARTMENT OF GEOLOGY, UNIVERSITY of Alberta, invites applications for appointment as Assistant Professor from Geologists who have completed their doctorate, preferably with specialization in one or more of the following fields: geomorphology, photogeology, hydrology, stratigraphy, paleontology. Initial salary $6,000 to $8,500; (8-month teaching year).—Application should be accompanied by a curriculum vitae and two letters of recommendation and addressed to Chairman, Department of Geology, University of Alberta, Edmonton, Canada.

UNIVERSITY OF AUCKLAND

NEW ZEALAND

SENIOR LECTURESHIP OR LECTURESHIP IN GEOGRAPHY

The Council invites applications for the above-mentioned post. Applicants should have special qualifications, teaching and research experience in either biogeography and climatology or cultural (especially economic) geography. The salary for a Senior Lecturer is £1,750 per annum, rising to £2,000 per annum, by annual increments, two of £100 and one of £50, and for a Lecturer £1,250 by £75 to £1,700 per annum. Commencing salary within the respective scales will be determined according to qualifications and experience. Travel and other removal expenses are allowed within certain limits.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in New Zealand and London, on February 17, 1961.

UNIVERSITY OF SYDNEY

LECTURESHIP AND SENIOR LECTURESHIP IN PURE MATHEMATICS

Applications are invited for the above-mentioned positions. Salary for a Lecturer is within the range £A.1,730 by £A.105 to £A.2,435 per annum; for a Senior Lecturer within the range £A.2,550 by £A.95 to £A.3,000 per annum and will be subject to deductions under the State Superannuation Act. In addition, in each case, cost of living adjustments will be paid. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. Under the Staff Members' Housing Scheme, in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application should be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on February 24, 1961.

UNIVERSITY OF SYDNEY

SENIOR LECTURESHIP AND LECTURESHIP/SENIOR LECTURESHIP IN PHYSICS

Applications are invited for the above-mentioned posts. One appointee will work with Professor C. N. Watson-Munro in the field of plasma physics in the Wills Thermonuclear Physics Department and the other appointee will work with Dr. B. Y. Mills in the Chatterton Astronomy Department. The salary for a Senior Lecturer is within the range £A.2,550 by £A.95 to £A.3,000 per annum; for a Lecturer within the range £A.1,730 by £A.105 to £A.2,435 per annum. In each case cost of living adjustments will be allowed. The salary is subject to deductions under the State Superannuation Act. The commencing salary and grade of appointment will be fixed according to the qualifications and experience of the successful applicant. Under the Staff Members' Housing Scheme in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on March 3, 1961.

NATIONAL INSTITUTE OF AGRICULTURAL BOTANY

Applications are invited for the following posts: (1) Two Research Assistants for work in the Official Seed Testing Station on (a) Seed Physiology and (b) Weed Dissemination. (2) Research Assistant to assist in studies on competition between cereals and other species. Applicants should have a degree in agriculture or botany, preferably at honours level. Starting salary for all three posts, for men and women, £560 at age 21, rising to a maximum of £1,240. Superannuation Scheme.

Further particulars and application form from M. G. Tozer, Secretary, N.I.A.B., Huntingdon Road, Cambridge.

CARDIFF HOSPITAL MANAGEMENT COMMITTEE

Senior Biochemist, suitably qualified, required at Sully Hospital (318 beds), near Penarth, Glam. Work will include co-operation with Surgical Department in investigation of biochemical problems. N.H.S. conditions and salary (£1,250 to £1,700 per annum)

Form of application from Group Secretary, 44 Cathedral Road, Cardiff.

COUNTY LABORATORIES LIMITED

Manufacturers of Brylcreem, Silvikrin, Macleans Toothpaste and many other well known toiletry products require for their Product Research Laboratory

Senior Biochemist—Honours Graduate to lead research on the Biochemistry and Physiology of skin and hair.

Excellent working conditions, Profit Participation and non-contributory Pension Schemes in operation.

Apply to Personnel Manager, County Laboratories Limited, Beecham House West, Great West Road, Brentford, Middlesex.

STANDARD TELECOMMUNICATION LABORATORIES

MILLIMETRE WAVES

We are actively engaged in programmes aimed at the realisation of coherent generators for millimetre and submillimetre wavelengths, and their exploitation in telecommunications.

Some of the approaches we are investigating are extensions of the microwave tube art, others represent new departures in the solid state field.

An extensive waveguide programme is under way.

We would like to meet physicists or engineers who feel that they could contribute creatively to any of these aspects of our work.

COHERENT OPTICAL GENERATORS AND MODULATORS

We are initiating a programme of research aimed at the realization of coherent optical and infra-red sources of radiation, and of efficient means of modulation and detection. The programme is aimed at a wide variety of ultimate uses.

We invite applications from physicists, preferably with experience in quantum mechanics and solid state theory, to participate in this interesting and challenging work.

THEORETICAL ANALYSIS

We would like to meet a mathematician or mathematical physicist who can command a considerable analytical ability combined with a strong sense of physical intuition. Experience in problems involving electron dynamics is desirable but not essential.

The problems involved are both difficult and stimulating. Excellent computing facilities are available.

S.T.L. has just moved into spacious new buildings near Harlow, where excellent housing is available.

Apply to Mr. P. J. Rogers, Personnel Manager, who will arrange an informal interview. Expenses of interview will be met.

Standard Telecommunication Laboratories Ltd.

LONDON ROAD HARLOW ESSEX

M&B

SENIOR PHARMACOLOGIST

MAY & BAKER LTD

DAGENHAM, ESSEX

Applications are invited from Pharmacologists for a senior post in the Research Laboratories of May & Baker Ltd. Applicants who should be not less than 30 years of age, should have had substantial research experience. The salary paid will depend on the ability and experience of the candidate, but it is considered that a suitably qualified candidate should justify a commencing salary of £1,500 per annum, and an outstanding research worker should eventually earn a salary within the range £2,000–£2,500 per annum. May & Baker research staff are encouraged to maintain academic contacts and to take part in meetings of scientific societies. Laboratory facilities in the new Research Institute are excellent. There is a Pension and Life Assurance scheme in operation.

Apply initially in writing to the Personnel Officer, quoting Reference No. 212/60.

LEIGH ELECTRONIC DEVELOPMENTS LIMITED

HAVANT, HANTS

LABORATORY TECHNICIAN

A Laboratory Technician is required with some experience of high vacuum work and some ability in glass blowing. O.N.C. qualifications will be advantageous. The successful candidate will be expected to take part in the development of prototype vacuum electronic devices.

A good salary will be paid, and in certain cases assistance towards rented housing can be given.

Applications to Regional Personnel Manager, Leigh Electronic Developments Limited, New Lane, Havant, Hants, quoting ref.: LED/23.

PARKE, DAVIS & COMPANY

require a LABORATORY TECHNICIAN for their PHARMACOLOGICAL RESEARCH LABORATORIES, preferably with some experience of general laboratory workshop practice, and building of electronic apparatus from specifications. Training will be given in the specific requirements on the job, with opportunities for further study.

Applicants should be 18+ years of age, preferably with a G.C.E. "A" level in Physics.

Terms of employment are attractive. They include a five-day, 37½-hour week, generous salary scale, and contributory life assurance plan. Staff restaurant.

Please apply to:
Personnel Manager,
Parke, Davis & Company,
Staines Road,
Hounslow, Middlesex.

PARKE, DAVIS & COMPANY

A vacancy exists in the DEPARTMENT OF PHARMACOLOGICAL RESEARCH for a QUALIFIED PHARMACOLOGIST with RESEARCH EXPERIENCE.

The work will be concerned with the search for new pharmacodynamic agents. Those with Ph.D., M.Sc., B.Sc., or B.Pharm. degrees, or equivalent qualifications, are invited to apply for this post.

The terms of employment with the Company are attractive. They include a generous salary, pension and life assurance plan, and a five-day, 37½-hour week.

Please apply:
Personnel Manager,
Parke, Davis & Company,
Staines Road,
Hounslow, Middlesex.

SENIOR TECHNICIAN II REQUIRED TO take charge of a Laboratory. Special experience in Bacteriology is necessary.—Applications, together with names of two referees, should be sent as soon as possible to Secretary, Forest Group H.M.C., Langthorne Road, E.11.

UNIVERSITY OF NEW ENGLAND
ARMIDALE, NEW SOUTH WALES
LABORATORY TECHNICIANS

Applications are invited for two positions of Laboratory Technician in the Faculty of Rural Science: Department of Physiology. Experience of laboratory procedures in haematology is desirable but not essential. The main research interest of the department is the physiology of erythrocytes. The successful applicant will have a responsible position in the team. Department of Livestock Husbandry. The technician will be primarily responsible for the development and functioning of a fleece measurement laboratory under the guidance of Dr. M. L. Ryder, but will be expected to assist with class preparations and research into wool growth, involving histological techniques. Experience in this field is desirable but not essential. The commencing wage will be fixed according to qualifications and experience up to £A.26 5s. 9d. per week (males) and £A.22 8s. 10d. (females) subject to future variations in the basic wage. Four weeks annual leave; liberal sick leave and long service leave. Fares will be paid and removal expenses up to £A.200. Laboratory technicians may enrol for a part-time B.Sc. degree.

Applications from within Australia and New Zealand should be forwarded to reach the Registrar, University of New England, Armidale, N.S.W., Australia, not later than February 10, 1961; applicants outside Australia and New Zealand should forward their applications to the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, by the same date. In the case of these candidates an additional copy should be forwarded to the Registrar, by air mail if necessary. Applications should give full particulars of qualifications and experience, together with the names of two referees.

UNIVERSITY OF MANCHESTER
RESEARCH ASSISTANT IN REGISTRAR'S OFFICE

An investigation is to be undertaken in the Registrar's Office into the application of electronic computing methods to such administrative processes as, for example, statistical analyses, registration of students, timetables for examinations, compilation and maintenance of records, etc. It is proposed to appoint a Research Assistant in the Registrar's Office for a period of about two years to take part in this investigation. Applications are invited from men or women graduates with experience of electronic computing for this appointment. Facilities will be available for the person appointed to work on ATLAS, the computing machine at present being developed in the computing machine laboratory. The salary will be in accordance with qualifications and experience, and the post will carry membership of the F.S.S.U. and children's allowance scheme. Duties to commence as soon as possible. Applications should be sent not later than January 14, 1961, to the undersigned, from whom further particulars and forms of application may be obtained.

VINCENT KNOWLES,
Registrar.

UNIVERSITY OF BRISTOL
I.C.I. RESEARCH FELLOWSHIP

Applications are invited from qualified candidates of any nationality for an I.C.I. Research Fellowship in Chemistry, Biological Chemistry, Engineering, Pharmacology, Physics, or in a related subject, to which an appointment may be made during the current academic year. The appointment will date from October 1, 1961, and may be made for a period up to a maximum of three years. The salary will depend upon qualifications and experience, but will be within the range £800 to £1,100 per annum, together with, in appropriate cases, F.S.S.U. benefits and family allowances.

Applications, stating age, details of qualification and experience, publications, research work in progress and an outline of the proposed field of research, together with the names of two referees, should be received not later than March 1, 1961, by the Registrar, the University, Bristol 8.

FELLOWSHIPS AND ASSISTANTSHIPS for advanced degree students in the fields of metallurgy, ceramics and semiconductors. A new Materials Research Centre provides exceptional facilities for basic research and graduate studies in kinetics physical ceramics and metallurgy, imperfection studies in solids, physics of solids, thermodynamics and X-ray diffraction.—Applicants with degrees in mathematics, the physical sciences or engineering will be considered. Department of Materials Science, the Technological Institute, Evanston, Illinois.

COMMONWEALTH AGRICULTURAL BUREAUX

Applications are invited for a vacancy as Junior Mycologist at the Commonwealth Mycological Institute, Kew, from candidates with a good honours degree in botany, and postgraduate training in systematic mycology. A working knowledge of Latin and German is required, with Russian an added qualification. Salary scale £710 to £2,325 by annual increments with bars and an additional London weighting of £20 to £50. Starting salary according to age, qualifications and experience. For those aged 32 or under at time of appointment, up to two increments allowed for completed years of National Service and two extra increments after two years' satisfactory service. Provision for superannuation.

Further information from the Secretary, Commonwealth Agricultural Bureaux, Farnham House, Farnham Royal, Bucks, England, to whom applications should be made not later than March 31, 1961. Government employees should apply through their Governments.

HAREFIELD HOSPITAL
HAREFIELD, MIDDX.

SENIOR LABORATORY TECHNICIAN
(Grade II)

required for the above General and Chest Hospital with special experience in haematology and blood transfusion work.

London weighting payable.

Applications, with names of two referees, to the Hospital Secretary.

CHARING CROSS HOSPITAL GROUP

HOSPITAL PHYSICIST (SENIOR GRADE)

Applications are invited for a new appointment in connection with the installation of teletherapy equipment in an extension of the radiotherapy isotope laboratory at Fulham Hospital, W.6. The work will involve collaboration in clinical research, using radioactive substances. Whitley Council salary and conditions.

Applications, with names of two referees, to House Governor, Charing Cross Hospital, W.C.2.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. A vacancy exists in the Physics Department, Sutton, Surrey, for a Biochemist to join a team engaged in the study of trace metal metabolism using radioactive tracer techniques. Candidates should possess a first- or second-class honours degree in biochemistry or chemistry and the possession of a higher degree would be an advantage. Salary in accordance with M.R.C. scales in the range £1,100 to £1,300.—Applications, giving the names of two referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 300/G/8.

THE DIRECTOR OF THE POULTRY Research Centre in Edinburgh invites applications for two posts concerned with Cancer Research. (1) A Qualified Electron Microscopist, with a biological background to investigate problems relating to cancer. Salary up to £1,450 according to qualifications and experience. Superannuation. (2) A Research Assistant, to collaborate with the Director in investigations relating to the physiological effects of controlled environments. A good honours degree is required and candidates should have some research experience. Salary £905. Superannuation.—Applications, with names of three referees, should be made to the Director of the Poultry Research Centre, King's Buildings, West Mains Road, Edinburgh, 9, within two weeks.

BRITISH PETROLEUM COMPANY LIMITED has a vacancy for a Chemist at the Research Centre, Sunbury-on-Thames. Applicants should have an honours degree in chemistry and not be more than 30 years of age. A postgraduate training is desirable with experience in the manipulation of electron spin resonance equipment and interpretation of the measurements. The job requires an interest in the application of electron spin resonance techniques to a variety of physicochemical systems including, for example work with a linear accelerator on radiolysis of hydrocarbon and sulphur compounds. Salary according to age, qualifications and experience. Non-contributory pension fund. Housing scheme, luncheon club. Removal expenses and settling-in allowance payable in certain cases.—Write, giving full details, quoting reference H.5377, to Box 6480, c/o Hanway House, Clark's Place, E.C.2.

UNIVERSITY OF NOTTINGHAM
I.C.I. RESEARCH FELLOWSHIPS

Applications are invited for Imperial Chemical Industries Research Fellowships in Chemistry (including Agricultural Chemistry), Physics, Pharmacy, Engineering, Metallurgy and related subjects, tenable at the University of Nottingham. A number of appointments may be made as from October 1, 1961, with a normal tenure of three years. The salary will be within the scale £800 to £1,100 per annum, depending on qualifications and experience. Fellows will have status as members of the academic staff and will be eligible for F.S.S.U. benefits and children's allowances.

Further particulars and forms of application may be obtained from the Registrar, to whom applications must be returned not later than March 1, 1961.

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Lecturer or Assistant Lecturer in Applied Mathematics. Salary Scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475. Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton to whom applications (seven copies from United Kingdom applicants) should be sent not later than February 10, 1961.

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Lecturer or Assistant Lecturer in Pure Mathematics. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475. Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton to whom applications (seven copies from United Kingdom applicants) should be sent not later than February 10, 1961.

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF ELECTRONICS

Applications are invited for an additional post of Lecturer or Assistant Lecturer in Electronics. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475. Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton, to whom applications (seven copies from United Kingdom applicants) should be sent not later than February 28, 1961.

SENIOR RESEARCH FELLOWSHIP
tenable for three years at the
CHEMICAL DEFENCE EXPERIMENTAL ESTABLISHMENT
Porton, near Salisbury, Wilts

Applications are invited from graduates in Biochemistry a Ph.D. degree and at least three years postgraduate research experience (preferably in enzyme chemistry). A working knowledge of histology and histochemical methods would be an advantage. Remuneration according to individual merit in the range of £1,275 to £1,575. Superannuation under F.S.S.U. Prior to expiry of Fellowship the holder, if under 31, can be considered for a permanent (pensionable) post.

Application forms from War Office, C.13(c)3, Adelphi, John Adam Street, London, W.C.2, for return by January 31, 1961.

THE BRITISH JUTE TRADE RESEARCH Association has vacancies for Chemists to join a group studying the fundamental chemistry of cellulosic fibres. The qualifications required are an honours degree in chemistry, with an interest in the physical or organic branches. Some previous research experience is desirable, although not essential. The position is superannuated and good salaries will be paid.—Suitably qualified men and women are invited to write to the Secretary, British Jute Trade Research Association, Kinnoull Road, Kingsway West, Dundee, for further information.

TEACHING ASSISTANTSHIPS FOR PH.D. candidates beginning September 1. Annual stipends up to $3,200. Research in: red blood cell chemistry, enzyme chemistry, plant biochemistry, protein physical chemistry, lipid metabolism, clinical chemistry.—Write to: Head, Department of Biochemistry, University of Alberta, Edmonton, Canada.

UNIVERSITY OF MANCHESTER

Applications are invited for the following posts in the Department of Physics of the Faculty of Science: Lecturer in Physics (Experimental); Lecturer in Theoretical Physics; Assistant Lecturers in Physics. The research interests of the Department include Nuclear and High-Energy Physics, Optics, Low Temperature and Molecular Physics. Duties to commence as soon as possible. Salary scales: Lecturer, £1,050 to £1,850 per annum, initial salary according to qualifications and experience; Assistant Lecturer, £800 to £950 per annum. Membership of F.S.S.U. and Children's Allowance Scheme.

Applications must be sent not later than January 14, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained. Applications by airmail letter in the first instance will be received from overseas candidates, who should state the names and addresses of at least three persons to whom reference can be made.

STOKE MANDEVILLE HOSPITAL
AYLESBURY

Assistant Biochemist required in the Area Pathology Laboratory based at the above hospital. Applicants should possess first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C. Whitley Council conditions of service. Salary £925 to £1,150 per annum after (for new entrants only) a probationary period. The post offers a wide variety of experience in a well-equipped and pleasant laboratory.

Applications, giving full details of qualifications, etc., together with names of two referees, to be forwarded to the Administrative Officer as soon as possible.

NORTHAMPTON COLLEGE OF ADVANCED TECHNOLOGY
LONDON

READER IN APPLIED NUCLEAR PHYSICS

The Governing Body invites applications for the above appointment in the Department of Applied Physics. Applicants should possess high academic qualifications and considerable research experience in this branch of applied physics. Salary scale: £1,836 rising to £2,148 per annum.

Further particulars and a form of application can be obtained from the Secretary, Northampton College of Advanced Technology, St. John St., London, E.C.1.

UNITED NEWCASTLE UPON TYNE HOSPITALS

Applications are invited for a post of Medical Laboratory Technician in the Department of Dermatology at the Royal Victoria Infirmary, Newcastle to assist in research on skin physiology, cell metabolism and serum protein disturbances in immunological reactions. Salary and conditions of service will be those agreed by the Whitley Council for the Health Services.

Applications, giving two referees, should be sent to the House Governor and Secretary, Royal Victoria Infirmary, Newcastle.

QUEEN'S UNIVERSITY OF BELFAST

Applications are invited for an I.C.I. Fellowship in one of the following subjects: Chemistry, Biochemistry, Physics, Engineering, Chemotherapy and related subjects. Appointment will date from October 1, 1961. The stipend, depending on age, qualifications and experience, will be within the range £800 to £1,100. F.S.S.U. and family allowances.

Applications should be sent not later than March 1, 1961, to the Secretary, Academic Council, Queen's University of Belfast, from whom further particulars may be obtained.

KING'S COLLEGE HOSPITAL
DENMARK HILL, S.E.5
BACTERIOLOGY DEPARTMENT

A Biochemical Research Assistant is required for work on the action of chloroquine. Experience in technique for the study of tissue metabolism and in animal work is desirable. The appointment will be for one year in the first instance. Salary range £700 to £800 per annum according to experience.

Applications, stating age, qualifications and previous experience, together with the names of two referees, should be sent to the undersigned by January 17, 1961.

J. D. BANKS,
House Governor.

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF GEOLOGY

Applications are invited for the post of Lecturer or Assistant Lecturer in Geology. Candidates should have a particular interest in sedimentary petrology. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475. Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton to whom applications (seven copies from United Kingdom applicants) should be sent not later than February 3, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Pure Mathematics. The initial salary will be within the range £800 to £1,250 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than February 3, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Ref.: CV/N.

COMMONWEALTH AGRICULTURAL BUREAUX

Scientific Assistant to prepare abstracts. Scale £710 to £1,800 with F.S.S.U.; starting salary according to age, qualifications and experience. University degree, preferably with a knowledge of genetics; ability to write concise English; knowledge of at least two foreign languages.

Apply in handwriting to Director, Commonwealth Bureau of Animal Breeding and Genetics, King's Buildings, Edinburgh 9, by January 21, 1961.

UNIVERSITY OF LIVERPOOL

Applications are invited for a Lectureship or Assistant Lectureship in the Department of Applied Mathematics. The initial salary will be within the range £800 to £1,350 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of two referees, should be received not later than January 31, 1961, by the Registrar, the University, Liverpool, from whom further particulars may be obtained. Ref.: CV/N.

UNIVERSITY OF READING

Applications are invited for a post of Lecturer in the Department of Education; applicants should possess a degree in science, preferably in Chemistry. The appointment will date from September 30, 1961.

Further particulars may be obtained from the Registrar (Room 22, O.R.B.), the University, Reading, by whom applications must be received not later than February 1, 1961.

BIRKBECK COLLEGE
(UNIVERSITY OF LONDON)

Applications are invited for the post of Assistant Lecturer in Physics. Salary scale £800 by £50 to £950 per annum, plus London allowance of £60 per annum.

Further particulars should be obtained from the Secretary, Birkbeck College, Malet Street, W.C.1. Closing date for applications: January 31, 1961.

COMMONWEALTH BUREAU OF PASTURES and Field Crops, Hurley, Berkshire, requires Scientific Assistant (abstractor) with degree in agriculture or natural science, and a knowledge of languages. Salary in scale £690 to £1,750. Age, qualifications and experience considered when fixing starting salary. Superannuation.—For further details and application form, apply to Director. Applications to be received by February 7.

SUB-EDITOR WITH EXPERIENCE, RE quired by established scientific publishing firm (London). Salary by arrangement according to qualifications.—Write to Box No. 941, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

PHYSICIST WITH ELECTRONIC AND/OR instrument experience, and preferably at least honours degree, required for fundamental and applied research in a growing organization concerned with building materials.—Write for form of application to Box No. 937, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

BIOCHEMIST

A Biochemist is being sought by the Malayan Pineapple Industry Board to conduct research into the organic constituency of pineapple. The officer will be required to relate field conditions affecting fruit quality, such as nutrition or disease, to fruit organic constituency; evolve improved fruit processing techniques and apply them on a laboratory scale; develop quality standards for raw and processed fruit with defining quantitative tests; and investigate fruit and plant by-products, such as juice and leaf fibre. The Biochemist, in addition to an extensive knowledge and experience in biochemistry, should be familiar with the basic principles of organic, inorganic, physical and analytical chemistry. Experience with ion exchange resins and chromatography is essential. Experience in food technology will be an important advantage. The post is a first appointment in Processing Chemistry and at the outset the appointee will become head of this Department within the Board's Research Organization. He will be located at Tampoi, five miles north from Johore Bahru, Malaya. The appointee will be required to contribute to the Board's provident fund (5 per cent of salary). Free medical care is provided for the appointee and his family; free dental care is provided for the appointee; first class air fares (or equivalent) and a reasonable baggage allowance are paid for the appointee and his family on taking up the post. Housing and basic furniture are also provided by the Board at low rentals. The salary offered will fall in the range M$15,000 (= U.S.$5,000; £S.1,750) to M$18,000 (= U.S.$6,000; £S.2,100) per annum.

Applications, in duplicate, should be forwarded to the Chairman, Malayan Pineapple Industry Board, P.O. Box No. 35, Johore Bahru, Malaya, before February 15, 1961. Applications should include a recent photograph (returnable) of the applicant, the names and addresses of three technical referees, together with certified transcripts of University courses taken and degrees received.

WESTERN INFIRMARY
GLASGOW

Senior Technician required for the Radiotherapy Department of the above Infirmary. Qualifications and salary scale in accordance with Whitley Council conditions for Technicians in Hospital Physics Departments.

Applications should be sent to the Medical Superintendent, Western Infirmary, Glasgow, W.1.

UNIVERSITY OF ALBERTA
DEPARTMENT OF CHEMISTRY
TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

RESEARCH BIOLOGIST, GRADUATE, male or female, age 23 to 30 required for supervising laboratory tests in new Fungicides at Chesterford Park Research Station, near Saffron Walden, Essex. Highly interesting post carrying good conditions of employment. Five-day week, canteen facilities and Sports and Social Club available. Pension Scheme in operation.—Write, giving full particulars and quoting number 1594 to Personnel Manager, Fisons Pest Control Ltd., Harston, Cambridge.

JOHN INNES INSTITUTE REQUIRE AN Assistant with chemical background to help in biochemical investigations in potatoes in the Department of Potato Genetics. The appointment will be in the Assistant Experimental Officer grade, and a Pass Degree or equivalent qualification is required. Salary will be in the range £520 to £745 per annum according to age and experience. Superannuation.—Applications, with the names of two referees, should be addressed to the Secretary, Bayfordbury, Hertford, not later than February 7, 1961.

THE LONDON HOSPITAL, WHITECHAPEL, E.1, has vacancy for Biochemist (basic grade) in the Metabolic Ward Laboratory.—Applicants should have B.Sc. honours degree in chemistry or biochemistry. The successful applicant will be trained for a career in hospital biochemistry and opportunities for developmental work in biochemical analyses will be provided, so some postgraduate experience of these is desirable.—Write to House Governor, giving names of two referees.

UNIVERSITY OF NEW BRUNSWICK

FREDERICTON, N. B., CANADA
DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Assistant or Associate Professor in the Department of Mathematics. Applicants should possess an honours degree in mathematics and preferably some postgraduate experience in research or teaching. Commencing salary will be according to qualifications.

Further particulars may be obtained from the Head of the Department.

DURHAM COLLEGES IN THE UNIVERSITY OF DURHAM

Applications are invited for the post of Lecturer in the History of Science from October 1, 1961. The salary attaching to the appointment will be £1,050 to £1,850 a year.

Applications (three copies), together with the names of three referees, should be sent not later than January 31, 1961, to the Secretary, 38 North Bailey, Durham, from whom further particulars may be obtained.

RESEARCH INSTITUTE (ANIMAL VIRUS Diseases), Pirbright, Surrey, invites applications: (1) For an appointment in the Tissue Culture Section. Applicants should have an honours degree in bacteriology or zoology and have experience of culture techniques applied to mammalian tissue. Salary in Principal Scientific Officer grade, £1,600 to £2,325 or Senior Scientific Officer grade, £1,250 to £1,590, depending on age, qualifications and experience. Superannuation under F.S.S.U. House available for married applicant. Applications to the Secretary. (2) From young graduate physicists or physical chemists for a post in the Biophysics Department. The successful candidate will be engaged upon the application of a variety of physical-chemical techniques to the study of viruses and related biological systems, and will be encouraged to work for a higher degree. Current methods of investigations include electronmicroscopy, ultracentrifugation, light scattering and X-irradiation, etc. Interest rather than experience is required at this stage. The appointment will be made according to age and experience in the Scientific Officer grade, £690 to £1,175, or Senior Scientific Officer grade, £1,250 to £1,590. Superannuation under F.S.S.U. House available for married applicant.—Applications to the Secretary.

A PLANT PHYSIOLOGIST IS REQUIRED to join the Biochemistry Section of Twyford Laboratories Ltd., Twyford Abbey Road, London, N.W.10, to engage in basic investigations. Some research experience in the field of plant biochemistry or in botanical microtechnique is desirable. Salary according to experience and qualifications; pension scheme.—Apply to Secretary at above address.

JOHN INNES INSTITUTE REQUIRE AN Animal Attendant (male or female) to be responsible for experimental stocks of rats, mice, and rabbits in the Department of Cell Biology. Some previous experience in the care of handling of small animals will be an advantage. Salary £350 to £675 per annum according to age and experience.—Apply in writing to the Secretary, Bayfordbury, Hertford, Herts, with names of two referees, by January 31, 1961.

GEOLOGISTS. FOUR POSITIONS AVAILable to teach in the fields of mineralogy, petrology petrography, paleontology, stratigraphy, structural geology, economic geology and geophysics. Good opportunities for research. Adequate salary. Two-year contract, renewable.—Inquiries, with complete credentials, to Escola de Geologia, Universidade da Bahia, Salvador, Bahia, Brazil. Courses in Portuguese, Spanish, English or French.

LECTURES AND COURSES

UNIVERSITY COLLEGE LONDON

FREE PUBLIC LECTURES, SPRING TERMS, 1961

Monday, January 16 at 5.30 p.m., "Biochemistry and Biology of Enzymes in Cancer," by Professor F. Bergel. Thursday, January 19, 26 at 5 p.m., "Nucleotide Anhydrides and Oligonucleotides," by Dr. A. M. Michelson. Thursday, February 23, March 2 at 5 p.m., "Recent Advances in the Chemistry and Biochemistry of Glycogen and Starch," by Dr. W. J. Whelan.

Complete list of public lectures (including lunch-hour lectures) from Publications Office, University College London, Gower Street, W.C.1 (Stamped envelope required).

SURREY COUNTY COUNCIL

KINGSTON TECHNICAL COLLEGE
POSTGRADUATE LECTURE COURSES
SPRING TERM 1961

"Chemical Spectroscopy." Nine Lectures on Thursday evenings at 7 p.m. commencing January 19, 1961. The Lecturers will include Dr. V. S. Griffiths, Dr. L. J. Bellamy, Dr. J. H. Callomon, Dr. N. Sheppard, Dr. D. J. Millen, Professor R. T. Williams, Dr. A. J. B. Robertson, Mr. P. D. Ainsley.

"Theories of Valency." A correlation of modern ideas. Six lectures on Wednesday evenings at 7 p.m., commencing January 25, 1961, to be given by Dr. T. M. Dunn of University College, London.

Details and registration forms from the Head of the Chemistry Department, Kingston Technical College, Fassett Road, Kingston-upon-Thames.

UNITED KINGDOM ATOMIC ENERGY AUTHORITY

ISOTOPE SCHOOL

Basic four week courses of instruction in the measurement, handling and use of radioisotopes commence January 9, June 12 and November 13, 1961. Medical Courses commence April 10 and September 18.

Special courses for Chemists, Biochemists, Biologists and Engineers are included in the 1961 programme.

Full particulars and forms of application may be obtained from: Registrar, Isotope School, Wantage, Berkshire.

MIDDLESEX COUNTY COUNCIL

Education Committee
HARROW TECHNICAL COLLEGE
Northwick Park, Watford Road, Harrow
USES OF RADIOACTIVE MATERIALS IN INDUSTRY, MEDICINE AND RESEARCH

Twelve weekly lectures, commencing Tuesday, January 3, at 7 p.m.

Further particulars from the College.

TRADE ANNOUNCEMENTS

SILICA CONES AND SOCKETS, VITREOus silica tubing, polished silica discs and glazed sheet always in stock.—Custom built silica/quartz apparatus from Jencons, The Silica Centre, Mark Road, Hemel Hempstead, Hertfordshire. Boxmoor 4641.

GRANTS & SCHOLARSHIPS

NUFFIELD FOUNDATION

DENTAL FELLOWSHIPS AND SCHOLARSHIPS

The Nuffield Foundation invites applications, from citizens of the United Kingdom, for Fellowships and Scholarships in Dentistry. To help the advancement of teaching and research in the United Kingdom on dental health and disease, the Foundation is prepared to award a number of Fellowships: (i) to enable selected men and women with dental qualifications to receive such additional training in pure and applied science as is desirable to fit them for an academic career in dentistry (but not to obtain a medical qualification), and (ii) to enable selected university graduates in medicine and science to receive training that will qualify them to undertake teaching and fundamental research on dental health and disease. The Foundation is also prepared to award a limited number of Scholarships to assist students of outstanding ability attending a university dental school to devote one or two years to further studies of the basic sciences.

All applications must first be endorsed by the executive authority of the appropriate dental or medical school or scientific faculty of a university in the United Kingdom. They must be received by the Foundation by March 1 in the case of Fellowships, which are awarded once a year; and by January 31 and June 30 in the case of Scholarships, which are awarded twice a year. Copies of the conditions of both Fellowships and Scholarships and the application forms are obtainable from the Director, the Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

L. FARRER-BROWN, C.B.E.,
Director of the Nuffield Foundation.

THE ROYAL SOCIETY

BROWNE RESEARCH FUND

The Council of the Royal Society is prepared to consider applications for personal grants to enable individuals to carry out research in marine biology. Applications are receivable from persons already holding posts in universities or other institutions to enable them to undertake specific research at a marine biological laboratory for periods up to twelve months, on the understanding that their university or other positions would meanwhile be kept open for them. On this occasion applicants are advised that grants normally will be limited to persons having special reasons for requiring a grant during 1961. Applicants should give the following information: (i) The period for which a grant is required (and any special reasons why a grant is required during 1961) (ii) The sum which is required, including an estimate of the loss of salary which would be incurred during absence from duty. (iii) Evidence that leave of absence for the necessary period would be likely to be obtained. (iv) A summary of the research which it is proposed to carry out. (v) The names of not more than two referees who will support the application. (Where the applicant is a Fellow of the Royal Society no referee need be named).

In accordance with Mr. Browne's bequest, preference will be given to those who propose to work on purely scientific problems rather than to those whose work would be primarily directed towards an economic end. Applications should be sent to the Assistant Secretary, the Royal Society, Burlington House, Piccadilly, London, W.1, not later than January 31, 1961.

McMASTER UNIVERSITY

GRADUATE SCHOLARSHIPS IN PHYSICS

Applications are invited for Graduate Scholarships in the Department of Physics, McMaster University, from students qualified to register in courses leading to the M.Sc. and Ph.D. degrees. These scholarships may be supplemented by Departmental Assistantships, requiring ten hours per week service during the seven-month academic year, to provide a yearly income (less fees) of $1,875 to $2,175.

Graduate Calendars and application forms for graduate study may be obtained from the Secretary of the Faculty of Graduate Studies. Further information concerning the types of research in progress and application forms for scholarships may be obtained from Professor H. E. Duckworth, Chairman, Department of Physics, Hamilton College, McMaster University, Hamilton, Ontario, Canada.

UNIVERSITY OF SYDNEY

F. H. LOXTON POSTGRADUATE STUDENTSHIPS OR SCHOLARSHIPS

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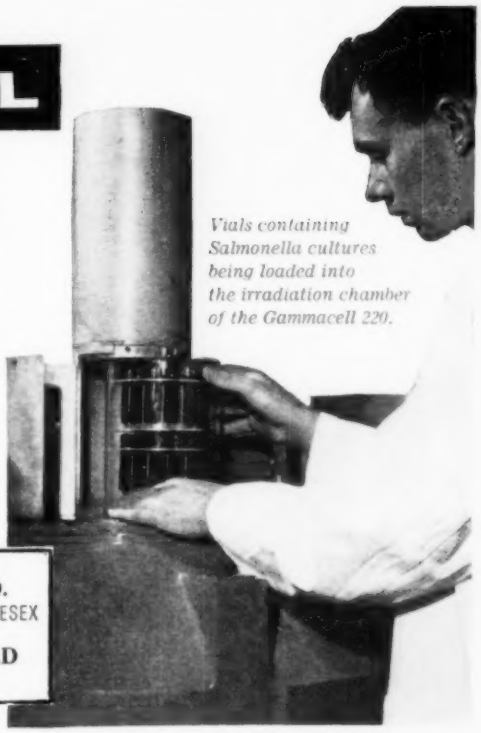

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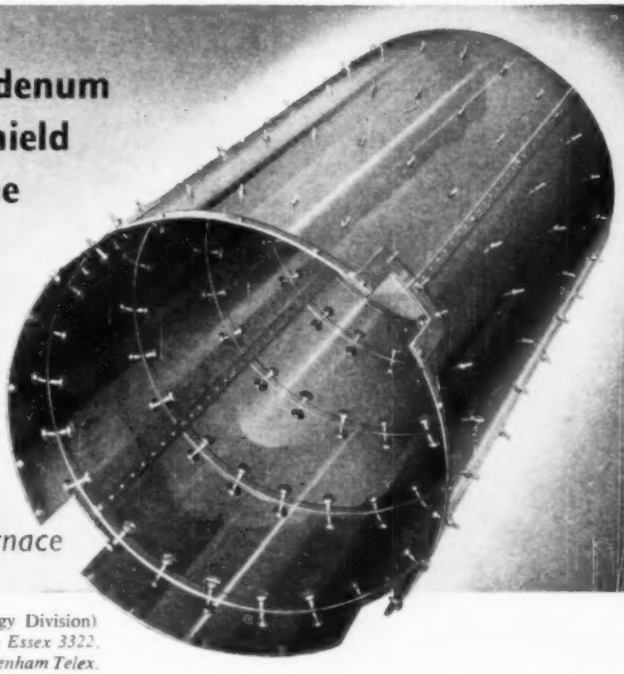

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